federal register

Friday
December 2, 1988

Part IV

Environmental Protection Agency

Proposed Guidelines for Exposure-Related Measurements and Request for Comments; Notice

ENVIRONMENTAL PROTECTION AGENCY

[FRL-3484-8]

Proposed Guidelines for Exposure-Related Measurements

AGENCY: Environmental Protection Agency.

ACTION: Proposed guidelines for exposure-related measurements and request for comments.

SUMMARY: The U.S. Environmental Protection Agency (EPA) is proposing risk assessment guidelines for exposure-related measurements, and invites public comment.

The Proposed Guidelines for Exposure-Related Measurements are intended to assist those who must recommend, conduct, or evaluate an exposure assessment. These proposed guidelines were developed as part of an interoffice guideline development program under the auspices of EPA's Risk Assessment Forum. The current proposal incorporates comments from external and internal peer reviewers. EPA's Science Advisory Board (SAB) will review these proposed guidelines at a meeting to be held on December 2, 1988. For further details regarding the SAB review, contact Jan Kurtz at (202) 382-2552.

DATES: Comments must be postmarked by March 2, 1989.

ADDRESS: Comments may be mailed or delivered to: Michael A. Callahan, Director, Exposure Assessment Group, Office of Health and Environmental Assessment (RD-689), U.S. Environmental Protection Agency, 401 M Street SW., Washington, DC 20460.

Inspection and copies: References, support documents, and other relevant materials will be available for inspection and copying at the Public Information Reference Unit (202-382-5926), EPA Headquarters Library, 401 M Street SW., Washington, DC, between the hours of 8:00 a.m. and 4:30 p.m.

FOR FURTHER INFORMATION CONTACT: John Segna or Michael Callahan, telephone: 202-475-8909.

SUPPLEMENTARY INFORMATION: In its 1983 book "Risk Assessment in the Federal Government: Managing the Process", the National Academy of Sciences recommended that Federal regulatory agencies establish "inference guidelines" (1) to promote consistency and technical quality in risk assessment, and (2) to ensure that the risk assessment process is maintained as a scientific effort separate from risk management. A task force within EPA accepted that recommendation and requested that Agency scientists begin to develop such guidelines.

In 1984, EPA scientists began work on risk assessment guidelines for carcinogenicity, mutagenicity, suspect developmental toxicants, chemical mixtures, and exposure assessment. Following extensive scientific and public review, these five guidelines were issued on September 24, 1986 (51 FR 33992-34054).

The guidelines proposed today continue the guidelines development process initiated in 1984. Like the guidelines issued in 1986, the new proposal sets forth principles and procedures to guide EPA scientists in the conduct of Agency risk assessments and to inform Agency decision-makers and the public about these procedures. In particular, the guidelines emphasize that risk assessments will be conducted on a case-by-case basis, giving full consideration to all relevant scientific information. This case-by-case approach means that Agency experts study scientific information on each chemical under review and use the most scientifically appropriate interpretation to assess risk. The guidelines also stress that this information will be fully presented in Agency risk assessment documents, and that Agency scientists will identify the strengths and weaknesses of each assessment by describing uncertainties, assumptions, and limitations, as well as the scientific basis and rationale for each assessment.

The guidelines are formulated in part to bridge gaps in risk assessment methodology and data. By identifying these gaps and the importance of the missing information to the risk assessment process, EPA wishes to encourage research and analysis that will lead to new risk assessment methods and data.

Work on the Proposed Guidelines for Exposure-Related Measurements began in 1986. The draft guidelines were developed by Agency work groups composed of scientists from throughout the Agency, and the drafts were peer-reviewed by experienced professionals from environmental groups, industry, EPA, and other governmental agencies. During the public comment period, reviewers are requested to comment specifically on the guidance for interpreting contaminated blanks vs. field data (section 2.5.4), the interpretation of data at or near the limit of detection (section 3.3.2), approaches to assessing uncertainty (section 3.4) and, the Glossary of Terms. Public comment is also invited on the following questions: Should these guidelines be combined with the 1986 guidelines? Is the current state-of-the-art in making measurements of population activities for the purpose of exposure assessment advanced to the point where the Agency can construct guidelines in this area? Given that these guidelines are not necessarily a protocol or detailed literature review, is the level of detail of these guidelines useful and appropriate, especially in the area of statistics?

After SAB and public comment, Agency staff will prepare summaries of the comments and analyses of major issues presented by the commentors. The comments will be considered by EPA's Risk Assessment Forum and Risk Assessment Council in the development of final guidelines.

Date: November 22, 1988.

John A. Moore,

Chairman, Risk Assessment Council.

Contents

1. Introduction

1.1 Purpose of the Guidelines.
1.1.1. Intended Audience.
1.1.2. Organization of the Guidelines.
1.1.3. Role of Technical Support Documents.
1.2. Exposure Assessment.
1.3. Sources of Measurement Data.
1.3.1. Direct Measurement of Exposure.
1.3.2. Biological Monitoring for Reconstructive Exposure Assessment.
1.3.3. Measurements for Predictive Exposure Assessment
1.4. Quality Assurance and Quality Control Requirements.
1.5. Other Requirements.

2. Guidelines for Making Measurements for Exposure Assessments

2.1. Responsibilities of the Exposure Assessor.
2.2. Defining Objectives.
2.3. Developing a Sampling Strategy.
2.3.1. Direct Exposure Measurements.
2.3.2. Reconstructive Exposure Measurements.
2.3.3. Predictive Exposure Measurements.
2.4. Setting Data Quality Objectives.
2.5. Sampling Plan.
2.5.1. Sampling Design.
2.5.2. Sampling Location and Frequency.
2.5.3. Sampling Duration.
2.5.4. Sample Preparation.
2.6. Evaluating Uncertainty.
2.6.1. Sampling Errors.
2.6.2. Laboratory Analysis Errors.
2.6.3. Data Manipulation Errors.
2.6.4. Reporting Data Near the Detection Limit.
2.7. Quality Assurance, Control, and Assessment.
2.8. Selection and Validation of Analytical Methods.
2.9. Background Level.

3. Guidelines for Using Measurements in Exposure Assessments

3.1. Use of Measurement Data in Making Inferences for Exposure Assessments.
3.2. Relevance of Measurement Data for the Intended Exposure Assessment.
3.2.1. Direct Measurement of Exposure.
3.2.2. Reconstructive Exposure Assessment.
3.2.3. Predictive Exposure Assessment.
3.2.4. Measurements and Modeling.
3.2.5. Use of Surrogate Data in Pesticide Exposure Assessment.
3.2.6. Combining Measurement Data Sets from Various Studies.
3.3. Adequacy of Measurement Data for the Intended Exposure Assessment.
3.3.1. Quality Assurance and Quality Control for Previously Generated Data.
3.3.2. The Role of Limit of Detection (LOD) Values in Measurements Used to Estimate Exposure.
3.4. Evaluation and Description of Uncertainty in the Use of Measurements.
3.4.1. Assignment of Limits of Uncertainty to Data.
3.4.2. Statistical Analysis of Data.
3.4.3. Decision Analytic Approach for Expert Opinion.

Glossary of Terms

References

1. Introduction

1.1. Purpose of the Guidelines

In 1984, EPA organized a new program to ensure scientific quality and technical consistency in the Agency's risk assessments. Included in the program's goals was the development of Agencywide guidelines for risk assessment. The first group of five guidelines was issued in 1986 and included The Guidelines for Estimating Exposures (U.S. EPA, 1986a). The Proposed Guidelines for Exposure-Related Measurements is a companion and supplement to the Guidelines for Estimating Exposures.

The Guidelines for Estimating Exposures were developed to help avoid inadvertent mistakes of omission. They present the risk assessor with a set of questions to be considered in carrying out an exposure assessment and provide a procedural framework for estimating the degree of human contact with a chemical of concern. The Guidelines for Estimating Exposures set forth internal Agency procedures that facilitate consistency by developing common approaches to exposure assessments and by promoting the quality and accuracy of science underlying EPA exposure assessments.

As stated in the Guidelines for Estimating Exposures, "Ideally, exposure measurements are based on measured data. EPA recognizes that gaps in data will be common, but the Guidelines will nevertheless serve to assist in organizing the data that are available, including new data developed as part of the exposure assessment. In the absence of sufficient reliable data and the time to obtain appropriate measurements, exposure assessments may be based on validated mathematical models. Whenever possible, exposure assessments based on modeling should be complemented by reliable measurements." Comments received on the Guidelines for Estimating Exposures, including comments from EPA's Science Advisory Board (SAB), suggested a supplement dealing in more detail with how to make and use measurements in exposure assessment. In accord with these suggestions, the Agency prepared the Proposed Guidelines for Exposure-Related Measurements.

This document focuses primarily on chemical measurements in various physical and biological media. The guidelines are intended to help exposure assessors make informed choices regarding collection and interpretation of these types of data. Other types of exposure-related measurements (e.g., activity profiles) are not considered in detail here.

The Proposed Guidelines for Exposure-Related Measurements (hereinafter Guidelines) are not intended to serve as a step-by-step instructional guide, but to convey general principles. They represent a collection of information already refined by consensus approval. As the Agency performs more exposure assessments and incorporates various novel approaches, these Guidelines will be revised.

1.1.1. Intended Audience

These Guidelines are intended to assist those who must recommend, conduct, or evaluate an exposure assessment. Exposure assessment is a multidisciplinary process that should reflect the combined input of analytical and environmental chemists, biologists, engineers, statisticians, and others as appropriate. To ensure a credible exposure assessment, the assessor must be familiar with the site or program-specific needs and the factors that affect how well these needs will be fulfilled.

Important aspects to be considered when generating new data (i.e., making measurements) include sampling plans, field activities, and analytical methodologies. Exposure assessors will enhance their expert judgment with sample designs that provide objective measurements. The purpose of sampling an environmental medium, or of sampling exposures directly for an individual, or of sampling tissues or body fluids, is to make an inference about the nature of quality of the whole medium, population, or absorbed dose. Statistics, while a useful tool, cannot alone provide the rationale for the link between the sample and the whole. It is the exposure assessor, as builder of the assessment, who must provide the explanation and justification for this link, usually through carefully laid out logic as to why the sample is accurate and representative. Statistics, and the help of a statistician, however, are often essential parts of establishing the link between the sample and the population of inference.

When evaluating data (i.e., using exposure-related measurements) exposure assessors should carefully examine the relationship between the population on which the measurements were made and the population about which inferences are desired. Another matter to be considered and understood is the possible difference between statistical significance and practical significance. The former term relates to whether observed differences could be the result of the variability of the data used in a decision process. The latter relates to whether the difference, if real, would be of practical importance. For a given set of circumstances, measures of statistical significance should not vary from one assessor to another because they are calculated using established procedures, while statements on practical significance are very likely to vary from assessor to assessor since they are matters of opinion.

1.1.2. Organization of the Guidelines

These Guidelines consist of three parts. The introduction describes some general aspects of exposure assessment and some major sources of measurement data used in exposure assessment. The second chapter discusses the making (i.e., generation) of measurements for exposure assessments including the role of the exposure assessor, sampling plans, uncertainty analysis, quality assurance, quality control, and method selection. The third chapter describes the use of measurements in exposure assessments including evaluation of uncertainty in the use of measurements, the role of limit-of-detection values, and the use of surrogate data.

1.1.3. Role of Technical Support Documents

It is impracticable to create guidelines that give specific step-by-step instructions for every situation. The assessor should consult technical support documents, such as those referred to in these Guidelines, for more specific information.

BEST COPY AVAILABLE

1.2. Exposure Assessment

The National Research Council (NRC) in 1983 described risk assessment as containing some or all of the following four steps: *Hazard identification* (the determination of whether a particular chemical is or is not causally linked to particular health effects), *dose-response assessment* (the determination of the relation between the magnitude of exposure and the probability of occurrence of the health effects in question), *exposure assessment* (the determination of the extent of human exposure before or after application of regulatory controls), and *risk characterization* (the description of the nature and often the magnitude of human risk, including attendant uncertainty).

Once a dose-response relationship is established, and often this is done in a controlled situation such as a laboratory, one can make statements such as, "if the dose is 'x,' then the response should be 'y.'" A major problem confronting risk assessors when trying to apply the dose-response relationship to an actual "real-world" problem is the question of what dose to as representative of the actual situation. The primary purpose of an exposure assessment is usually to estimate the real-world dose value to use in a dose-response relationship.

The EPA Guidelines for Estimating Exposure (U.S. EPA, 1986a) define exposure as the contact with a chemical or physical agent. The magnitude of this contact is determined by measuring or estimating the amount of an agent available at the exchange boundaries (i.e., lungs, gastrointestinal tract, skin) during some specified time. Once the agent is absorbed through these boundaries, the amount crossing the boundary becomes the absorbed dose. Exposure assessment is the qualitative or quantitative determination/estimation of the magnitude, frequency, duration, and route of exposure. Exposure are sometimes referred to in the literature in terms of "administered dose" or "applied dose," which describe contact with the organism, but not absorption. These terms tend to be confusing and should not be used to describe exposure if avoidable. Exposures assessments often present not only the exposures, but also the absorbed doses, which can be calculated from exposure if the absorption fraction is known (see the Glossary of Terms).

Over the last decade, exposure assessors have generally approached the evaluation of real-world exposures in three ways: by trying to measure the exposure directly while it is taking place ("the direct measurement approach"), by trying to reconstruct an absorbed dose from evidence within an organism after the exposure and absorption have taken place ("the reconstructive approach"), or by trying to make estimates of the distribution of the chemical and the organism separately, then linking them ("the predictive approach"). All of these approaches involve measurements of some kind, and the measurements used in these approaches to determine or estimate exposure are generally termed "exposure-related measurements." This term applies to measurements taken for use in an exposure assessment, whether or not they measure actual exposures directly, or directly provide information upon which exposure will ultimately be estimated.

1.3. Sources of Measurement Data

This section describes some of the methods currently used to provide reliable measurements for exposure assessment needs. The methodologies discussed below focus on direct measurement of exposure, measurement of biological markers, and measurements for characterization of media for predictive assessments. These Guidelines will not discuss the collection of data on population activity patterns, although it is recognized that these data play an important role in exposure assessment.

The reader should keep in mind that the measurements discussed in sections 1.3.1 through 1.3.3 share s similarity in that for most of them, a substance or medium is being analyzed for chemical content. However, the *use* of the resulting measurement data is fundamentally different for the three different approaches to exposure assessment, and therefore considerations in *making* these measurements vary also.

1.3.1. Direct Measurement of Exposure

Direct measurement of exposure measures the contact of a chemical with an organism (human or nonhuman) while it occurs, by measuring the chemical concentrations at human physical exchange boundaries (skin, lungs, etc.) as a function of time (e.g., throughout a day) to obtain an exposure profile. A number of individual profiles can be statistically aggregated to make statements about the exposure profiles for human or nonhuman populations, provided the individuals sampled have a known relationship to the entire population.

As the name implies, the direct measurement method relies essentially on measured data. The best-known example of the direct measurement of exposure is the radiation dosimeter, a small badge-like device worn in areas where exposure to radiation is possible. The dosimeter effectively measures exposures to radiation while it is taking place, then indicates when a preset level has been exceeded. Another example of direct measurement of pollutant exposure is provided by the Total Exposure Assessment Methodology (TEAM) studies (U.S. EPA, 1987a) conducted by EPA. In the TEAM studies, a small pump with a collector and absorbent is attached to a person's clothing and measures the exposures to airborne solvents or other pollutants while the exposure takes place. The absorbent cartridges are then analyzed for a variety of chemicals. A third direct measurement example is given by the carbon monoxide (CO) studies done by EPA in the 1980s, where a small CO measuring device was carried by a number of people over several days (U.S. EPA, 1984a). The device had a recording capability which allowed the assessor to analyze the exposure to CO over that time period. In all three of these examples, the key to direct measurement techniques is that the measurements must be taken at the interface between the person and the environment and measure the exposure while it is taking place.

1.3.2. Biological Monitoring for Reconstructive Exposure Assessment

Another method, yielding useful measurement data for reconstructive exposure assessments, involves biological monitoring. Biological tissue or fluid measurements that reveal the presence of a chemical may indicate directly that an exposure has occurred, provided the chemical is not a metabolite of other chemicals. There has been much interest in relating biological sample levels to exposure, particularly for occupational exposure where chemical concentrations are high enough to permit easier detection.

Four types of measurements using biological monitoring can be used to evaluate the amount of a chemical in the body:

1. Measurement of the concentration of the chemical itself in various biological tissues or fluids (blood, urine, breath, hair, adipose tissue, etc.) (body burden).

2. Measurement of the concentration of one or more of the biotransformation products (metabolites) of the chemical.

3. Measurement of a biological effect that occurs as a result of human exposure to the chemical (e.g., alkylated hemoglobin) (types of biomarkers).

4. Measurement of the amount of a chemical bound to target molecules (e.g.,

BEST COPY AVAILABLE

DNA adducts or chromosome aberrations) (types of biomarkers).

The results of biomonitoring can be used to estimate the amount of chemical uptake during a specific interval if the relationship between uptake and the markers selected is known (i.e., pharmacokinetics are known) and if background levels before the exposure interval are known.

Reconstructive exposure assessment relies heavily on measured data. However, the data on body burden or biomarker values cannot be used directly for exposure assessment unless a relationship can be established between these levels and absorbed dose, and interfering reactions (e.g., from metabolism of nonrelated chemicals) can be accounted for or ruled out. Biological monitoring for exposure assessment usually involves sampling tissues or fluids for the purpose of making inferences about absorbed dose.

1.3.3. Measurements for Predictive Exposure Assessment

In predictive exposure assessment, the assessor attempts to match, or link, individuals or collections of individuals with the concentrations of chemicals or agents they are contacting. Usually, the assessor addresses the characterization of the individuals or population separately from the characterization of the chemical or agent. Population characterization involves identifying those individuals who are exposed and the activities (habits) that bring them into contact with the chemical or agent. This may involve demographics, survey statistics, behavior observation, activity diaries, or other means of obtaining this information. Although population characterization may involve measurements, these measurements are fundamentally different from the chemical/media characterization discussed in these Guidelines, and therefore will not be specifically discussed further here.

Measurements employed in characterizing the chemical or agent in predictive exposure assessments are quite varied, but they all share a common purpose: to use sampling to make inferences about the distribution of chemical/agent concentrations in the media being sampled. Measurements are often used as inputs to models. Once the concentration distribution has been estimated or measured, this information can be combined with the population characterization to estimate exposure.

The following are a few examples of the types of measurements used in predictive exposure assessment to characterize the concentrations of chemicals or agents in various media. *Fixed location monitoring* has been used by the Agency and other groups to provide a record of pollutant concentration at one spot over some length of time. Nationwide air and water monitoring programs have been established to provide continuous monitoring of pollutant concentration so that "baseline" values in these environmental media can be documented. *Measurements in environmental media* can also be done in focused studies which look for specific chemicals or agents in specific places and time. *Indoor air measurements* simply refer to the geographic zone monitored. There are valid reasons for differentiating indoor measurements from outdoor ones, since when performing an exposure assessment, the considerable time spent indoors for most persons needs to be linked with the concentrations they are exposed to indoors. The home, office, automobile, or other defined areas are often called *microenvironments*, and are used in predictive exposure assessment to better link chemical concentrations with individuals or populations. *Breathing zone measurements*, usually associated with industrial hygiene studies of worker exposure, refer to measurements taken by a fixed location device situated at approximately head height at or near where the worker spends a substantial amount of time. Note that this differs from direct measurement, since the monitor is fixed rather than moving with the worker. *Food and drinking water measurments* are often made to characterize these potential exposure pathways. General characterization of these media, such as market basket studies, shelf studies (where foodstuffs are taken from store shelves and analyzed), or drinking water quality surveys are linked in a predictive exposure assessment with the characterization of the individuals or population assessed. (Again, this differs from direct measurement of exposure, where measurements of food and drinking water are taken as split samples simultaneously as an individual is ingesting them.) *Source characterization measurements* usually refer to sampling to determine the rate of release of chemicals or agents into the environment from a point of emission such as an incinerator, landfill, industrial or municipal facility, or other source. Often these measurements are used to estimate emission factors, or a relationship between releases and operating parameters of a facility (x mg of chemical released per ton of waste burned, etc.). The release rates are often combined in a predictive exposure assessment with environmental transport and transformation (environmental fate) data or models, resulting in an estimate of the distribution of the release in the environment over time. This distribution must then be linked to individuals or populations before exposures can be estimated. *Consumer or industrial product analysis* is sometimes done to characterize the concentrations of chemicals or agents in products with which individuals came in contact. In predictive exposure asssessment, this information can be linked with population activities to estimate exposures, provided information is known about how much the individual actually comes in contact with the product. (For example, when holding a product, an individual does not usually contact the entire product, nor do the chemical additives immediately become available on the surface being contacted, etc.)

31.4. Quality Assurance and Quality Control Requirements

While the preceding discussion has described a number of types of measurements, all of them must provide sufficient proof of reliability. This proof is embodied in the form of quality assurance and Quality Control. The Agencywide quality assurance policy stipulates that every monitoring and measurement project undertaken by the Agency must have a written, approved Quality Assurance Project Plan (QAPjP) and Data Quality Objectives (DQOs).

EPA's Office of Research and Development (U.S. EPA, 1983) has published "Interim Guidelines and Specifications for Preparing Quality Assurance Project Plans", which describes the sixteen elements required in every QAP,P and establishes criteria for plan preparation, review, and approval. Every QAP,P should contain procedures that can be used to document and report precision, accuracy, and completeness of environmental measurements.

Individual EPA program offices have prepared more specific guidance based on this general guidance package.

1.5 Other Requirements

An exposure assessor must also be aware of other requirements that are important in specific types of assessments. For example, one must consider that in the process of obtaining direct measurements of exposure in all Federally-funded exposure studies that mandatory submission of a complete survey design to the Office of

Management and Budget (OMB) may be necessary. The guidelines for all such submissions are outlined in the Federal Paperwork Reduction Act (U.S. OMB, 1988).

2. Guidelines for Making Measurements for Exposure Assessments

2.1 Responsibilities of the Exposure Assessor

As noted in section 1.2, the exposure assessor's task is to obtain or estimate dose information representative of actual exposure situations for use in the dose-response relationships which are generally established under controlled conditions, usually in a laboratory. Since dose involves both the organism and the chemical, obtaining representative dose information involves establishing a link between the organism and the chemical. Again, exposure assessors commonly attempt to make this link in any of several ways: by direct measurement, by predictive relationships involving individual study of the distribution of the organisms and chemical in time and space, or by reconstructing the dose after it has occurred. In most cases, the exposure assessor works from individual organism exposures and aggregates these to make statements, inferences, or conclusions about the exposure profiles of collections of individuals (subpopulations, populations, etc.).

In order to make these inferences and conclusions, the assessor often uses measurements along with the concept of sampling. A sample is a small portion of a whole (e.g., specimens of water from the entire drinking water distribution system, 10 cubic meter portions of air within a home, several individuals in a town of 25,000) intended to represent the nature or quality of the whole. The most important responsibility of the exposure assessor is to understand and explain the relationship between the measurement data (samples) and the conclusions drawn about exposure to the subpopulation or population being assessed (the whole).

Good planning, sound statistics, and adequate quality control will go a long way toward building that link between sample and whole. The ultimate utility of new measurements taken for exposure assessment is strongly influenced by sampling strategy (sampling locations, sampling frequency, sampling duration), quality assurance (e.g., sample preparation, handling, and preservation), and knowledge about systematic and random sampling errors (American Chemical Society, 1983). It is incumbent on the exposure assessor to be well informed and to participate in such decisions relating to the making of measurements so that the sampling process is relevant to the questions being asked of the assessor. In addition, the exposure assessor should be involved (along with an analytical chemist and statistician) in selecting the appropriate analytical methods. Likewise, the exposure assessor needs to be involved in quality assurance, control, and assessment. The following discussion is intended to assist the exposure assessor in the highly complex process of making measurements for exposure assessments. The subject areas described below are often interrelated and, even though the process of planning and executing exposure-related measurements is described in a sequential manner, the exposure assessor must recognize the interative nature of the entire process.

2.2 Defining Objectives

A critical choice which must be made early in the process of conducting exposure-related measurements is the decision regarding exactly what is to be measured, what data quality is required, and what resources are available to carry out the study. In order to accomplish this, the exposure assessor must first explicitly define the overall objectives including the type of assessment (i.e., direct, predictive, or reconstructive) that the study is intended to support, the approach to be followed, and the nature of the decisions that will be made based on the data. Studies can range form being scoping in nature, intended to develop a hypothesis for further testing, to detailed investigations for the purpose of deciding on remedial actions or to support regulatory decision-making. In every case proper planning prior to data collection is essential to ensure that the results of the study are consistent with the anticipated uses of the data.

To facilitate this planning, the exposure assessor should keep some basic questions in mind:

Why is the study being conducted? What questions (hypotheses) does the study intend to address and to what uses will the results be put?

Where does the study area begin and where does it end? Is the intent of the study to make inferences on a national, regional, or local scale?

Who is to be monitored? Will the study involve human and/or nonhuman populations? How are they to be identified, characterized, and stratified?

What substances and what media will be measured? What is known about the environmental fate as well as the fate of the substance within the receptor organism? What are the important exposure pathways? What is known about expected concentration levels, analytical methods, and detection limits?

What will the samples be collected? How frequently will the sampling be conducted? Is the intent to characterize exposure as a function of specified variables?

By addressing each of these questions, the exposure assessor will develop a clear and concise definition of study objectives that will form the basis for further planning. The following list of overall objectives illustrates the range of data requirements in terms of variety, quantity, and quality that will result from this process. Generally, the requirements and, therefore, the effort and associated costs increase as one proceeds down the list.

Example Study Objectives

Determining whether exposure occurs to support the need for toxicity testing.

Establish mean or peak exposures.

Establish the fraction of a given area or the percent of time that exposures exceed a particular level for purposes of demonstrating compliance or the need for remedial action.

Establish trends in exposures and the efficacy of risk management decisions.

Determine exposures as a function of location, population characteristics, activity patterns, or other factors.

2.3. Developing a Sampling Strategy

Having decided on the overall objectives of the measurements effort, the exposure assessor should then be prepared to advance to the next level in planning the study which involves making decisions regarding the types of measurements to be undertaken. Data from health or ecological effects studies can be used in deciding such issues as which route of exposure or which medium is most important to sample and the level of detection that is required. Frequency considerations might depend on whether the effects studies have examined average concentrates of the chemical of interest or the effect of peak exposures. Much more frequent sampling must be undertaken to determine peak exposures versus average exposure. Besides the number of sampling locations and samples to be collected, the frequency of sampling is the most significant cost multiplier in a sampling program.

As discussed in section 1.2, there are three approaches useful in exposure assessment. Each of these three approaches (namely, direct measurement methods, predictive methods, and reconstructive methods) has particular strengths and weaknesses and each has different data requirements. When direct measurement of exposure is not possible, indirect methods (i.e., predictive or

reconstructive) are used, the most common being predictive methods. In general, predictive methods link sources, environmental pathways, monitoring data, and population (individual) activity patterns through use of models and exposure scenarios to estimate exposures. The reconstructive approach is almost always combined with one of the other methods to form a better assessment. In fact, many exposure assessments are a combination of two or all three approaches; the TEAM study is a good example of an assessment that combines direct measurement with the microenvironmental predictive approach and breath measurements for the reconstructive approach (U.S. EPA, 1987a).

2.3.1. Direct Exposure Measurements

Directly measuring human exposure to environmental pollution is a rapidly emerging science. In such studies measurements are made of the actual pollutant concentrations contacting a person's body by essentially using split samples of the air breathed, the food eaten, and the water consumed, and by using patch or other techniques to estimate dermal exposure. Availability of appropriate measurement methodology is, therefore, an essential element in planning a direct exposure monitoring study. Existing methodology developed for occupational exposure or environmental monitoring may not be adequate to meet the special demands of direct measurement of exposure. This is especially true with air or respiratory measurements where the monitoring device must be sufficiently small and lightweight to be worn or carried by the person or animal. Although much has been accomplished in certain areas, such as the development of small personal monitors for carbon monoxide (CO) and volatile organic chemicals (VOCs) and the development of sensitive methods for sampling exhaled air, new technology must be developed to accurately determine the exposure to many, if not most, of the airborne pollutants of concern at nonoccupational levels. A highly useful bibliography covering models, field data, and emerging research methodologies which should be consulted in planning direct exposure studies is "Total Human Exposure and Indoor Air Quality" (U.S. EPA, 1988a).

2.3.2. Reconstructive Exposure Measurements

Measurements in support of reconstructive exposure assessments can be characterized as being one of four types: (1) Measurement of the chemical or (2) its metabolites in biological media, (3) determination of a biological effect related to the internal dose, e.g., determination of alkylated hemoglobin, and (4) measurement of the amount of chemical bound to the target molecules e.g., (DNA adducts) or other molecular changes (e.g., chromosome aberrations). Collectively, these measurements are known as biomonitoring of exposure. The principal advantage of biomonitoring is it confirms entry of an environmental pollutant into an organism and, thereby, removes a major assumption in most current exposure assessments (i.e., that the material enters the body) and thus considerably strengthens risk assessments. Theoretically, biomonitoring can integrate total intake to the body from multiple sources and, if the substance is stable, it can integrate exposure over time. For many chemicals of interest, application of biomonitoring to exposure and risk assessments is limited by the availability of appropriate analytical techniques, cost of the assay, and sufficient understanding of the relationship between external exposure, body burden, internal dose, and adverse effects.

In general, most reconstructive environmental studies have focused on monitoring chemicals that are moderately to highly persistent in human tissues. This is based on the reasoning that there is greater potential for exposure and, therefore, adverse effects to result from exposure to more persistent chemicals. Occupational exposure studies have, on the other hand, focused more on transient exposure levels, and the TEAM studies have used breath measurements to help evaluate exposures to VOCs.

The kinds of specimens to be collected in a reconstructive study will vary depending on the following factors: accessibility, prevention of contamination, and existence of analytical procedures. Accessibility is determined first by whether materials will be collected from living persons or cadavers. From living persons typical sampling involves blood, urine, hair, fingernails, and feces. For cadavers (or surgical patients), one can sample adipose tissues, liver, kidney, and other organs. For example, many studies include liver because it is both an accumulating organ and a site of pollutant detoxification and hence a site where many pollutants are likely to be found. It is also present in large enough quantities to obtain individual samples and it tends to be more homogeneous in its distribution of trace substances. Adipose tissue is the ideal depository for lipophilic compounds where many chemicals, including chlorinated pesticides and biphenyls, are concentrated to levels that can be three orders of magnitude more than in the blood. Adipose tissue is available in large quantities from cadavers and is quite homogeneous in its trace contaminant distribution. Blood and urine are often chosen as indicators of recent as well as long-term exposure. They can be sampled repeatedly from the same individual, over a period of years. Samples can be readily obtained, are inexpensive, and information about lifestyle and occupation of the donor can provide clues to exposure routes and sources of the toxicants.

2.3.3. Predictive Exposure Measurements

As mentioned previously, direct exposure measurements may not be feasible in a given situation due to cost, time constraints, unavailability of direct measurement methods for the chemicals of interest, or when the assessment of past or future exposures is desired. Presently, predictive methods, which attempt to link sources, environmental processes, ambient concentrations, target organisms, and activity patterns through models and exposure scenarios, are the most widely used for the Agency's risk assessments.

Although the environmental media are primarily responsible for the wide dispersion of anthropogenic chemicals that reach the environment and sometimes serve as major reservoirs of pollutant residues, the mere presence of a substance within an environmental medium does not indicate the extent to which exposure might occur. It is worth emphasizing here that ambient concentrations of a pollutant are not exposures to a pollutant. Ambient pollutant levels can give distorted estimates of exposure levels for many pollutants by failing to account for other sources of exposure. Moreover, ambient pollutant concentrations fail to account for time-activity patterns that affect exposure in segments of the population (i.e., there is no exposure if the organism is not present). Ambient measurements only indicate the amount of a chemical potentially reaching the exposed individual, and these data must be combined with other information through the use of environmental fate models and exposure scenarios to come up with realistic exposure assessments.

The exposure assessor should use caution in applying long-term monitoring data to specific exposure assessments, since the strategy that was used in siting the particular stations in the network may not correspond to the strategy needed to answer the questions at hand.

For example, although NASQAN (National Stream Quality Accounting Network) stations are located all across the nation, their siting is not based on a probability sample of stream locations designed to reflect water quality (U.S. Government Accounting Office, 1986). Likewise, aerometric monitoring sites are usually established to measure compliance with air quality standards rather than produce a statistically representative data base from which valid inferences of population exposure can be drawn. When ambient monitoring data are needed for an exposure assessment, the optimum approach is to site the sampling stations to address the specific objectives of the exposure assessment. However, this may be impracticable due to time or resource limitations, and existing monitoring locations may be used but only after the assessor has examined the purpose and design of the existing network and its appropriateness for providing the requisite data.

Air Measurements: Air pollutants exist, usually at trace levels, in the atmosphere in one or more physical states. These pollutants may be present as gases or vapors, as surface or bulk constituents of aerosol particles and droplets, or as constituents of cloud liquid water. The low concentrations (typically, in the ppt to ppb range) of most substances poses particular problems for separation and detection. In planning ambient air monitoring studies, the exposure assessor must recognize that for some air pollutants (especially primary pollutants, e.g., CO, as well as a variety of volatile organics) actual human exposures are not well represented by outdoor measurements but are better represented by a series of microenvironmental measurements (see section 3.2.3), including indooor measurements.

Vapor pressure and polarity are the two most important properties governing the succees of sampling organic compounds from air. These properties govern whether the chemical will be found in the gaseous, condensed, or adsorbed phase and will affect the ability to separate, identify, and quantify its concentration. For compounds having medium-to-high vapor pressures, components of interest are usually concentrated from large volumes of air with a solid sorbent material. Collection of whole air samples in stainless steel canisters, which have been specially electropolished to prevent decomposition of the collected compounds, has become an attractive alternative to sorbent sampling. Low vapor pressure compounds are normally associated with particles, and filtration of large volumes of air is the usual means of sampling. Recently, the status of a number of important techniques for sampling air have been reviewed (American Chemical Society, 1988); the exposure assessor should consult this review and the references contained therein for a detailed discussion of their advantages and disadvantages.

Surface and Ground Water Measurements: Water is a major vehicle whereby chemical pollutants are transported and transformed to other substances. Concentrations within a given water body may fluctuate widely as a function of rate and turbulence of flow. Natural water bodies can be very difficult to sample because of large diurnal, seasonal, and local variations. In the case of ground water, one of the toughest questions to answer is "How to obtain a sample that is representative of the aquifer" because of the heterogeneity and complexity of the matrix. Several references describing sampling techniques have been reviewed recently (American Chemical Society, 1988), and these should be consulted by the exposure assessor in planning such studies.

Soil and Sediment Measurements: Soils often exhibit extreme variability even within a small area. Variations of properties such as pH and organic carbon content within soil types can significantly alter the environmental behavior of chemicals so that their persistence, mobility, extractability, and bioavailability are altered. The interpretation of soil analysis is further complicated by the fact that concentrations of a particular substance in soils may bear little immediate relationship to its exposure potential. Guidance on performing soil monitoring studies has been developed (U.S. EPA, 1984b) and should be consulted in planning such studies. Sediments have been repeatedly shown to accumulate toxic chemicals, and many chemicals reach higher concentrations in sediments than in the overlying water column. As in the case of soils, however, there are many questions regarding the bioavailability of sediment-bound chemicals and their significance to the biosphere. The sampling techniques most frequently used fall into two broad categories: bottom grab (dredge) sampling and core sampling. Guidance for designing, implementing, and overseeing a sediment sampling program is available (U.S. EPA, 1985i).

Other Measurements: In addition to environmental concentration measurements, predictive exposure assessments use data on the physical/chemical properties of the substance, its production, use, and disposal patterns, release rates to specific media, environmental fate, exposed populations (size, location, activity patterns), concentrations in drinking water and food, bioavailability, and pharmacokinetics (see Table 3–1). It is beyond the scope of this document to provide a discussion of the considerations and approaches to measuring each of the factors that may go into a predictive exposure assessment. In reality, most predictive exposure assessments use a mix of measured, surrogate, and estimated data. Several methodology documents have been prepared (U.S. EPA, 1985a–h, U.S. EPA, 1986b) which, although not a series of "how-to" books, they do provide a catalogue of information sources and describe the use of the data in predictive exposure assessments. These documents provide a useful starting point in planning a study.

2.4 Setting Data Quality Objectives

All data are subject to some error, and errors can be introduced at various stages of data collection. Some types of error can be expressed quantitatively, but others can only be described qualitatively. The magnitude of the error assigned to a data set is related to data quality. As the magnitude of the error increases, the quality of the data decreases. Depending on the particular decisions that will be made with the data and the way the data will be used to support those decisions, specified levels of error may be tolerable. Data Quality Objectives (DQOs) are statements of the level of uncertainty that an exposure assessor is willing to accept in results derived from environmental data.

The setting of realistic data quality requirements is essential for proper planning because data of insufficient quality will have little value for problem solving, and data of excess quality may provide few, if any, additional advantages. DQOs should be established based on cost-effective consideration of the needs of the exposure assessment and the capability of the measurement process. Knowledge of the expected variability of the samples is required to estimate the number of samples to be taken and the number of measurements to be made on each sample.

Although the term connotes quality, DQOs also are intended to clarify the objectives of the study. They force the exposure assessor to crystallize

beforehand, in his or her mind, how the data will be used once it is collected.

The process of establishing the data criteria begins with the exposure assessor proposing limits (based on best judgment) on the level of uncertainty that will be acceptable for each conclusion to be drawn from new data, taking into consideration the resources available for the study. These limits include the uncertainty resulting from both the analytical and sampling components of the plan. Thus, the DQO process consists of an analytical component and a sampling component. The analytical component results in the selection of a cost-effective chemical analysis method that, when integrated with the selected sampling plan (see section 2.5), will satisfy the given objective. Frequently, the detection limit of a "standard" analytical method exceeds the concern level for the substance (this is particularly true for many suspected carcinogens) and, therefore, more costly procedures will be required. The sampling component involves specifying a sampling plan (including numbers, types, locations, and levels of sampling quality control) that takes into account the expected sample variability (may have to be determined by a pilot study), and, when combined with the analytical component, will provide data consistent with the DQOs.

The DQOs should include the following:

1. A description of the data to be obtained and the media from which samples will be collected.

2. A statement of the desired performance for each data-dependent element that specifies in as much detail as possible the acceptable probabilities associated with false positive and false negative situations of varying degrees of magnitude. This statement should indicate the level of uncertainty that can be tolerated if the result is to be included in a decision-making process.

3. A clear statement of the objectives of the study.

4. The scope of study objectives including the smallest part of the data set from which a separate result will be calculated, and the largest unit (area, time period, or group of objects) that the data are expected to represent.

5. A discussion of how the results will be tested, including the following: Statistics that will be used to summarize the data; any standards, reference values, or action levels to which the statistics will be compared; and a statement of the rationale for and specifics of the mathematical and/or statistical procedures that will be used to derive the result.

6. Initial estimates of the time and dollar resources expected to be expended for the data collection effort.

The quality of a data set is represented in terms of precision, accuracy, representativeness, completeness, and comparability. Only precision and accuracy can be expressed in purely quantitative terms. The other statistics are best expressed using a mixture of qualitative and quantitative terms. Brief descriptions of these terms are given below:

Precision—Precision is a measure of the reproducibility of the analyses under a given set of conditions. Specifically, it is a quantitative measure of the variability of a group of measurements compared to their average value. Sampling precision is determined by analyzing multiple samples chosen at random from the same population, i.e., collected at the same point in time and space so as to be considered identical. Analytical precision is determined by the analysis of separate aliquots of a homogenized sample or separate aliquots of a spiked matrix and its replicates. Precision is usually stated in terms of sample standard deviation, but other estimates such as the coefficient of variation (sample relative standard deviation), the range (maximum value minus minimum value), and the relative range are common. Analytical precision is much easier to control and quantify than sampling precision.

Accuracy—Accuracy is a measure of the correctness of the data that takes into account the variability and bias that may exist in a measurement system. Unlike precision, accuracy is difficult to measure for the entire data collection activity. Sources of error include the sampling process, field contamination, preservation, handling, sample matrix, and analysis. Accuracy can only be estimated by evaluating all sources of variability and bias, to that extent possible. Accuracy is usually determined by analysis of a well-characterized sample or reference material, or is stated in terms of the mean recovery determined by analysis of a matrix spike and its replicates.

Representativeness—Representativeness expresses the degree to which sample data accurately and precisely represent a characteristic of a population, parameter variations at a sample point, or an environmental condition. Representativeness is a qualitative parameter that is very important in the proper design of the sampling plan, since it is related to the relevance of the data to exposure (see section 3.2). Representativeness is best addressed by describing sampling techniques and the rationale used to select the sampling locations. Samples can be biased (based on existing data, surveys, observations, etc.) or unbiased (completely random or stratified-random approaches). Later, in using the data for exposure assessment, this information will help build the logical link between the samples and the characterization of the whole media (see section 3.1).

Completeness—Completeness is a measure of the amount of valid data obtained from a measurement system compared to the amount that was expected to be obtained under normal conditions. Completeness is usually expressed as a percentage. Site access, sampling problems, analytical problems, and the data validation process can all contribute to missing data. Missing data may reduce the precision of estimates, introduce bias, and lower the level of confidence in the conclusions. A completeness goal must be included in the process to make sure that enough data of sufficient quality are obtained from the measurement system to fulfill the objectives of the study.

Comparability—Comparability describes the confidence with which one data set can be compared to another. Comparability refers to such issues as using standard field and analytical techniques and reporting data in the same units. For this data collection step, the assessor must consider whether two or more data sets are comparable. For example, if more than one field team is collecting samples or more than one laboratory is analyzing the samples, equivalent methods must be used to ensure that everyone is measuring the same thing in the same way. In this manner conclusions may be drawn from the totality of existing data.

2.5. Sampling Plan

The quality of the analytical data used in an exposure assessment depends on the choice of the sample and the adequacy of the sampling and analytical programs. As discussed earlier, the exposure assessor must first have a clear understanding of the overall goals of the study and have decided on the nature of the sampling and the data quality objectives. Once this has been achieved one can then proceed to the development of the sampling plan.

A *sampling plan* is a set of rules or procedures that specify how a sample is to be selected and handled. An inadequate plan will often lead to biased, meaningless, or unreliable results; good planning, on the other hand, maximizes the efficient use of limited resources and is more likely to produce valid results.

2.5.1. Sampling Design

Sampling for the purposes of exposure assessment is a complex process. The

heterogeneous nature of the environment poses particular problems in obtaining a representative sample. The sampling design specifies the number and type of samples needed to achieve the data quality objectives. Factors to be considered in developing the sampling design include the study objectives, sources of variability (e.g., environmental heterogeneity in time and space, analytical variability) and their relative magnitudes, relative costs, and practical limitations of time, cost, and personnel.

Decisions are made regarding replication in time and space, compositing (combining several samples into one prior to analysis), and multiple determinations on a single sample. A statistical (or environmental process) model, which may be simple or complex depending on the circumstances, is used to allocate sampling effort in the most efficient manner. For example, consideration of sources of variability together with cost may suggest multiple analyses of individual samples in one case and single analyses of a large number of samples in another case.

Prior knowledge of environmental factors may suggest designs that take into account expected physical or spatial relationships. Stratified random sampling is one approach that involves subdivision of the sampling universe into strata (e.g., according to geographical region, soil type, etc.). Appropriate choice of strata leads to more efficient use of sampling resources compared with simple random sampling when prior knowledge is available. Kriging, developed initially for geostatistical applications, is a statistical interpolation method that uses models of the spatial correlation between measurements. It is particularly suited for developing contour map representations of, for example, chemical concentrations in soil. As with stratified random sampling, an appropriate choice of model allows more efficient use of sampling resources compared with simple random sampling. Model selection, however, involves professional judgment and therefore may be subject to criticism. The sampling approach should be thoroughly reviewed to identify its strengths and weaknesses prior to implementation. An example of both approaches being used in tandem is provided in "Data Quality Objectives for Remedial Response Activities" (U.S. EPA, 1987b), in which stratified random sampling is used in the initial phase of a site remediation investigation, followed by the use of geostatistical techniques to effectively target subsequent sample collection.

The difference between survey and experimental approaches should be recognized. The survey approach seeks to estimate exposure of a population based on the measured exposure of a statistically representative sample from the population. In some situations the study objectives may be better served by an experimental approach which seeks to describe the relationship between two or more factors, e.g., the relationship between house construction and a particular indoor air pollutant. In the experimental approach, experimental units are selected to cover a range of situations (e.g., different housing types) and do not reflect the frequency of those units in the population of ultimate interest. An understanding of the relationship between factors gained from an experiment can be combined with other data (e.g., distribution of housing types) to estimate exposure. An advantage of the experimental approach is that it may provide more insight into underlying mechanisms that may be important in targeting regulatory action. A properly conducted survey has the additional benefit, however, of providing representative estimates of population characteristics with known uncertainty. To justify the experimental approach one has to argue, as in all experimental work, that the relationships revealed by the experiment apply beyond the situation of the particular experiment.

A single study may use a combination of survey and experimental approaches and involve a variety of sampling techniques. Relevant EPA reference documents include "Survey Management Handbook", Vols. I and II (U.S. EPA, 1984c). A detailed description of methods for enumerating and characterizing populations exposed to chemical substances is contained in "Methods for Assessing Exposure to Chemical Substances", Vol. 4 (U.S. EPA, 1985d). Statistical input is essential during this planning stage to make the most efficient use of available resources and to ensure that the number and type of samples collected are likely to achieve the data quality objectives.

2.5.2. Sampling Location and Frequency

Factors to be considered in selecting possible sampling sites include population density, historical environmental sampling results, patterns of environmental contamination and variability (such as prevailing wind direction or stream flow), access to the sample site, types of samples, frequency and duration of sample collection desired, and health and safety of field personnel.

There are many sources of information on methods for selecting sampling locations. Schweitzer and Black (1985) and Schweitzer and Santolucito (1984) give statistical methods for selecting sampling locations, particularly for sampling ground water, soil, and hazardous wastes. A practical guide for ground-water sampling is also available (U.S. EPA, 1985h) as well as a handbook for stream sampling (U.S. EPA, 1986c).

The term *sampling frequency* indicates the time interval between the collection of successive samples. The type of sample to be taken and the physical and chemical properties of the chemical of concern will usually dictate the sampling frequency. For example, determining the concentration of a volatile chemical in surface water would require a higher sampling frequency than necessary for ground water because the chemical concentration of the surface water would be changing more rapidly.

The optimum number, spacing, and sampling frequency can best be estimated after a preliminary survey. Factors to be considered in determining the number of samples to be obtained include technical objectives, resources available, the schedule of the program, types of analyses, and the constituents to be evaluated. Examples for air, surface water, and ground water of the application of statistical techniques for determining the optimum number of samples required to give data with specific limits of confidence include Shaw et al. (1984), Sanders and Adrian (1978), and Nelson and Ward (1981). The best assurance of obtaining a good sampling plan is to rely on a professional statistician.

2.5.3. Sampling Duration

The duration of sampling depends on the analytical method chosen, the limits of detection, the physical/chemical properties of the analyte, chemical concentration, and knowledge of transport/transformation mechanisms. For example, sampling duration may be extended to ensure adequate collection of a low concentration chemical and may be curtailed to prevent the breakthrough of a relatively high concentration of volatile chemical. Also, duration of sampling is directly related to selection of statistical analyses, such as trend versus cross-sectional analyses.

2.5.4. Sample Preparation

A major analytical concern is to ensure that the samples are not biased by the introduction of field or laboratory contamination. If the validity of the

sample is in question, all the analytical results will be questionable. Field and laboratory spiked samples and blank samples should be analyzed concurrently to validate results.

While conducting the sampling plan, careful attention should be given to collecting, preparing, preserving, and analyzing samples according to the established protocols.

The method for interpreting and using the results from blank samples should be specified in the sampling plan. The following EPA documents provide examples.

For *volatiles and semivolatiles* the action in the case of unsuitable blank results depends on the circumstances and the origin of the blank. No positive sample results should be reported unless the concentration of the compound in the sample exceeds 10 times the amount in any blank for the following contaminants: methylene chloride, acetone, toluene, 2-butanone, and common phthalate esters. The amount for other volatiles and semivolatiles should exceed 5 times the amount in the blank (U.S. EPA, 1988b). If a compound is found in a blank but not found in a sample, no action is taken.

For *pesticides/PCBs* no positive sample results should be reported unless the concentration of the compound in the sample exceeds 5 times the amount in the blank (U.S. EPA, 1988b). If a pesticide/PCB is found in a blank but not found in a sample(s), no action is taken.

For *inorganics*, no positive sample results should be reported if the sample results are greater than the instrument detection limit (IDL) and less than 5 times the amount in any blank (U.S. EPA, 1988c). Any blank with a negative result whose absolute value is greater than the IDL must be carefully evaluated to determine its effect on the sample data.

2.6 Evaluating Uncertainty

In evaluating and reporting uncertainty associated with measurements, sampling errors, laboratory analysis errors, and data manipulation errors are three categories of errors that should be evaluated. These are discussed in the next sections.

2.6.1. Sampling Errors

There are two kinds of sampling errors: systematic errors (often referred to as biases) that result from the sampling process, and random errors that result from the variability of both the population and the sampling process.

A biased sample can result from faulty assumptions. For example, one may assume that only the liquid phase of an aquatic system is important and may therefore ignore colloidal matter, suspended material, and sediment. A biased conception of an environmental situation could thus result. Unfounded discrimination with respect to speciation (chemical and biological) is another example of sample bias. Experimental failure to realize a proper discriminatory feature of an assumption could be another source of bias. For example, sampling a "respirable" fraction of particles in an atmosphere depends both on an appropriate definition of what is respirable and the use of a sampling device that has the required size discrimination. The presence or absence of such biases must never be assumed without experimental evidence. A sampling operation can be biased by faulty calibration of critical components such as flow meters, thermometers, pressure sensors, sieves, or any device that influences the sample or is used to quantitatively modify a measured result.

Biases of a different kind can result from contamination, losses, interactions with containers, deteriorations, and displacement of phase or chemical equilibria. Sources of bias must be considered in every sampling operation. A good procedure is to develop a "bias budget" wherein individual items are evaluated for significance, quantitatively when appropriate. Tolerances should be established to hold them within acceptable bounds, and adequate calibrations should be made of all critical components.

2.6.2. Laboratory Analysis Errors

Generally, laboratory errors are smaller than sampling errors. Preparation of accurate calibration standards helps minimize measurement bias as much as possible, since calibration is a major source of systematic error in analysis. This requires standards that suitably match the samples of interest in both matrix and level of analyte of concern. Other sources include chemical operations such as sample dissolution, concentration, extraction, and reactions. Blanks arising from the chemical operations, storage and handling of samples, sampling and transfer lines, and laboratory environment (including its personnel) must be controlled and evaluated.

Another type of error in laboratory analysis is the uncertainty of intercomparison of standards and samples. The measurement system must be in a state of statistical control, i.e., it must be stable and capable of producing a limiting mean value; the individual observations must be randomly distributed around the mean, and they must have a stable variance. Furthermore, each individual observation must be independent of others in a data set.

A system is statistical control will be stabilized but not necessarily optimized. Accordingly, its standard deviation will need to be evaluated and monitored on a continuing basis.

2.6.3. Data Manipulation Errors

Uncertainties that arise from errors in data manipulation are due to the operation of the measurement process and can be evaluated experimentally. Blunders, however, cannot be evaluated, so sufficient care must be exercised to prevent them to the extent possible.

Data manipulation errors can be of several kinds. These include errors of calculation, errors of transposition, errors of transmission, use of wrong units, use of improper conversion factors, spatial or temporal averaging information loss, and misassociation errors that confuse samples and numerical results. A measurement program should have built-in mechanisms to detect these errors. These can include, where appropriate:

1. Proofreading and hand checking calculations.
2. Ion balance.
3. Mass balance.
4. Comparison of results found for similar samples.
5. Graphical plots.
6. Tests for outliers.

A data set should not be released until it has been screened for possible blunders. The quality assurance program should include a prescribed procedure for data release, and any request to bypass it (premature release of data) should be resisted.

2.6.4. Reporting Data Near the Detection Limit

Oftentimes, extrapolation methodologies applied to toxicological studies result in acceptable risk levels which necessitate measuring environmental concentrations at or near the limit of detection (LOD). The limit of detection is defined as the lowest concentration level that can be determined to be statistically different from a blank (American Chemical Society, 1983). Data measured at or near the detection limit have considerably more uncertainty associated with them than when measurable amounts are present. To understand what a reasonably certain measure or a reliable detection is, the exposure assessor must understand the method of measurement as well as the statistical approach that

was used to calculate the limit of detection. Different statistical approaches will produce different limits of detection. It is beyond the scope of this document to discuss the various methods for calculating limit of detection values. Instead, the assessor should consult a statistician and become familiar with the advantages and disadvantages of each method (e.g., Long and Winefordner, 1983).

As a general rule, the exposure assessor should report all data that contribute to an understanding of the true situation including the extent to which data have been adjusted for recovery or other factors. If the exposure assessor reports individual values, the American Chemical Society's Committee on Environmental Improvement (1983) recommends that:

1. If the measured value is less than the limit of detection, report "not detected" together with the value for the LOD.

2. If the measured value is larger than the LOD but smaller than the limit of quantification (LOQ), report "detected but not quantifiable" together with the value for the LOQ. The LOQ is the level above which quantitative results can be obtained with a specified degree of confidence.

3. If the measured value is greater than the LOQ, report the value and its uncertainty.

The American Chemical Society recommendation sets the LOD at 3 standard deviation units above the mean value of the blank responses and the LOQ at 10 standard deviations above the blank responses.

2.7. Quality Assurance, Control, and Assessment

Quality assurance is a system of activities designed to provide the producer or user of a product or service with the assurance that the product meets defined standards of quality with a stated level of confidence. The quality assurance process involves quality control and quality assessment.

Quality control is the overall system of activities whose purpose in to control the quality of a product or service so that it meets the needs of users. The aim is to provide quality that is satisfactory, dependable, and economical. A quality control program should include developing and strictly adhering to priciples of good laboratory practice, consistently using standard operational procedures, and following carefully designed protocols for specific measurement programs. Qualified personnel, reliable and well-maintained equipment, appropriate calibrations and standards, and close supervision of all operations are essential components of a sound quality control program. A quality control program should foster a measurement system that operates in a state of statistical control, which means that errors have been reduced to acceptable levels and have been characterized statistically.

Quality assessment is the overall system of activities whose purpose is to provide assurance that the overall quality control job is being done effectively. It involves a continuing evaluation of the products produced and the performance of the production system. Quality assessment describes those techniques used to assess the quality of the measurement process and the resulting data. The establishment of a system of control charts is considered the best way to monitor the performance of a measurement system. Control charts are plots of multiple data points from the same or similar samples (or processes) versus time. The relative variability of repetitive data can thus be visualized. These charts can also be used with reference materials, spiked samples, and surrogates as a means of assessing the accuracy of measurements.

Quality assurance begins with the establishment of data quality objectives and extends throughout the entire measurement process. Each laboratory should have a quality assurance program and, for each study, a quality assurance project plan (QAPjP). This plan should be complete and detailed and its language clear and unambiguous to preclude confusion and misunderstanding (U.S. EPA, 1983). The contents of the plan should include the following:

1. Statement of the data quality objectives for the monitoring effort.
2. Full description of the chemical to be analyzed.
3. Review of the analytical method selected, following the procedures discussed in section 2.8.
4. Description of the steps taken to verify and validate the method.
5. Verification and validation results.
6. Description and source of reference standards.
7. Field study design with rationale.
8. Quality assurance and quality control used throughout the study.
9. List of equipment and materials to be used in the field.
10. Description of the system used to ensure sample preservation and handling, traceability of instrumentation, samples, and data.

Examples of the last quality assurance and quality control procedure listed above include the following:

Sample Preservation and Handling—When immediate analysis of the collected sample is not possible, precautions should be taken so that the sample integrity is not altered. The assessor should store the sample in a manner that guarantees that the parameters to be measured are not altered. The container material should not interfere with the analysis of the specific parameters, and the holding times specified for the analytical procedure should not be violated unless it can be demonstrated that significant changes have not occurred.

Traceability of Instrumentation—All collection and measurement instrumentation should have a unique identification number. Maintenance, calibration, and use logs should be maintained.

Traceability of Samples—All samples should have a unique identification number that is traceable to information on the field site, monitoring location, and collection devices. An efficient way to trace samples is to employ a bar code labeling system. Under this system, samples are labeled with adhesive bar code labels to identify the samples and trace them through the sampling and analytical procedures.

Traceability of Data—Data should be documented and filed to allow complete reconstruction from initial field records to data archiving.

Audits should also be a feature of all quality assurance programs. A systems audit should be made at appropriate intervals to ensure that all aspects of the quality assurance program are operative. Performance audits in which a laboratory is evaluated based on the results of analyses of blind standard samples also provide valuable quality assessment information.

2.8. Selection and Validation of Analytical Methods

Selecting the most suitable method of analysis involves developing a chemical profile of the chemical of interest. This profile should identify the physical and chemical properties of the chemical, such as vapor pressure, water solubility, octanol-water partition coefficient, boiling and melting points, molecular weight, and other properties that help characterize the chemical.

There are several major steps in the method selection and validation process:

Step 1. Determination of Method Requirements

The method requirements are normally established by the assessor who needs environmental measurement data. The

requirements identify the substances of interest (analytes), define the matrices to be examined, and specify (quantitatively) the performance of the method and the reliability, confidence, and quality of the measurements needed.

Step 2. Method Selection and Testing

Existing methods should be reviewed to identify candidate methods that may be adequate to meet the needs of the assessor. The method detection limit (MDL), which is the lowest amount detectable with a stated level of confidence, is of particular importance for selection of an analytical method and must be considered in light of the needs of the risk assessment.

Step 3. Single Laboratory Testing

The candidate method, if new, is subjected to laboratory and field testing, as necessary, to characterize its performance adequately with respect to the requirements established in Step 1.

Step 4. Comparability Testing

An evaluation similar to that described for Step 3 is conducted by other laboratories participating in the study to verify the method write-up and to confirm the results and conclusions of the method characterization conducted in the Single Laboratory Testing.

Step 5. Final Method Description

The method description is revised to incorporate changes or clarifications determined to be necessary based on the testing in Steps 3 and 4.

2.9 Background Level

At some sites, background chemical contamination is significant and should be accounted for. Background is defined as chemical contamination due to a source other than the site under investigation. Background can be either natural or from man-made sources. The exposure assessor should try to define local background conditions of concern by observing nearby locations clearly unaffected by the site under investigation.

When differences between a background (control site) and a target site are to be determined experimentally, the sampling of the control site must be done with the same detail and care as for that of the target. Otherwise, the uncertainty of any difference can be limited by the data for the control.

3. Guidelines for Using Measurements in Exposure Assessments

3.1. Use of Measurement Data in Making Inferences for Exposure Assessments

As discussed in the previous two chapters, the primary purpose for making measurements and using data related to exposure assessments is to make inferences from the measurements (samples) to the whole. In predictive exposure assessments, the whole is usually a medium of interest such as outdoor air, drinking water, a consumer product, etc. Once characterization of the medium has been made (and this may include changes over time), a matched link to individuals or populations being assessed must be made, usually via use of exposure scenarios. In direct measurement of exposure, sampling of one individual's exposure must be related to the exporsures of a collection of individuals (the whole). This relationship may also include inferences about different times and locations from those in the sample (e.g., different cities, winter vs. summer, present vs. past). In reconstructive exposure assessment, the whole is usually the total absorbed dose over some period of the past, which is reconstructed from samples of various tissues, fluids, or other biomarkers; individual absorbed doses might then be used to make inferences about collections of individuals.

In all these cases, the exposure assessor must have a clear picture of the relationship between the sample and the whole. It is obvious that the sampling being done for exposure assessments does not always try to characterize the same thing as "the whole." For example, samples of an environmental medium such as surface water, which are useful in characterizing the medium itself, are not necessarily immediately useful for characterizing exposures from surface water. But the characterization of the medium (over space and time) can be used, along with the location and activities of individuals or populations, to estimate exposures. Because the samples taken for exposure assessment differ in what they are trying to characterize, a sample taken as a direct measure of exposure, for example, is qualitatively different from a sample of an environmental medium, and these are qualitatively different from a tissue or body fluid sample.

The concept that different measurements, all taken under the general category of "exposure-related measurements," cannot all be used in the same way is critical to using these data in an exposure assessment. It is the exposure assessor's primary responsibility to understand, explain, and justify the relationship between the sample data and the inferences or conclusions being drawn from the data in the assessment. In doing so, the assessor must evaluate data relevance, adequacy, and uncertainty. These topics are covered in sections 3.2, 3.3, and 3.4, respectively.

Inferences are generalizations that actually go beyond the information contained in the set of data. Inferences involve at least some subjectivity, since it is impossible to eliminate all elements of subjectivity no matter how objectively data are collected. The credibility of an inference is often related to the method used to make it and the amount of supporting data it is based on. A guess, for instance, is one type of inference, although an assessor or decision-maker is likely to place less confidence in this method as a predictor of real-world events or conditions than many other methods. Anecdotal information, that is, stories of the form "once I knew a situation where * * *", are somewhat better than guesses as predictors, but the assessor has only a limited knowledge of where in the distribution of real-world situations this anecdote is being drawn from. Professional judgment is usually a better predictor that either guesses or anecdotes, since it presupposes that a (sometimes substantial) data base of experience (i.e., a collection of anecdotes) is being used, even if this is not a formal data base.

Statistical inferences also are generalizations that actually go beyond the data set. Statistical inferences may take any of several forms (see any statistics textbook for examples), but unlike the types of inferences mentioned above, a statistical inference will usually state not only the inference, but a measure of how good the inference is. For that reason, statistical inferences (including inferences involving judgment; see section 3.3.3) are often preferable to guesses, anecdotes, or professional judgment alone in understanding, explaining, and justifying the inferences made in linking the samples with the characterization of the whole, provided the data are shown to be relevant and adequate.

3.2. Relevance of Measurement Data for the Intended Exposure Assessment

Since all of the approaches to exposure assessment involve exposure measurements to some degree [1], it is important that the proper "match" be made between the measurement data and the type of exposure assessment. As discussed in the previous chapter, the exposure assessment approach will often dictate the type of measurements needed if new data are being generated. More often, however, the exposure assessor has at least some data that

[1] Of course, it is always possible to do a predictive assessment based solely on models and assumptions, without a subsequent reality check, but even these assessments use models and model inputs which may ultimately be based on measurement in some form.

BEST COPY AVAILABLE

were collected from previous studies, either for exposure assessment purposes or (more often) for other purposes. In determining relevance of data for the intended exposure assessment (adequacy of the data is covered in section 3.3), the assessor must consider not only the type of data and what it might logically characterize, but also how this characterization relates to risk.

There are many types of measurement data that an assessor can collect or evaluate for an exposure study. The measurements themselves are samples, and the assessor must have a clear idea of what kinds of inferences may be made for each type of measurements and what assumptions need to be made to make those inferences. Table 3–1 gives some examples of different types of measurements, what these samples are usually used to characterize, and what additional information must be known before the data, inferences, and characterizations can be used in an assessment.

As Table 3–1 illustrates, different types of measurements may be relevant to characterizing a variety of exposure-related media and parameters. (Nevertheless, just because certain measurements may be used to characterize these media or parameters is not a guarantee that in a particular assessment the medium or parameter can be adequately characterized with the data at hand (see section 3.3).) In addition to determining relevance to characterizing media or parameters, the assessor must also determine the relevance of these media or parameters to the exposure assessment.

TABLE 3–1.—EXAMPLES OF TYPES OF MEASUREMENTS TO CHARACTERIZE EXPOSURE-RELATED MEDIA AND PARAMETERS

Type of measurement (sample)	Usually attempts to characterize (whole)	Examples	Typical information needed to characterize exposure
A. *Predictive Assessments:*			
1. Fixed Location Monitoring	Environmental medium; samples used to establish long-term indications of media quality and trends over time.	NASQAN,[1] water quality networks, air quality networks.	Population location and activities relative to monitoring locations; fate of pollutants over distance between monitoring and point of exposure; time variation of pollutant concentration at point of exposure.
2. Short-term Media Monitoring (including indoor air).	Environmental or ambient medium; samples used to establish a "snapshot" of quality of medium over relatively short time.	Special studies of environmental media, indoor air.	Population location and activities (this is critical since it must be closely matched to variations in concentrations due to short period of study); fate of pollutants between measurement point and point of exposure; time variation of pollutant concentration at point of exposure.
3. Source Monitoring of Facilities.	Release rates to the environment from sources (facilities) (often given in terms of relationship between release amounts and various operating parameters of facility).	Stack sampling, effluent sampling, leachate sampling from landfills, incinerator ash sampling, fugitive emissions sampling, pollution control device sampling.	Fate of pollutants from point of entry into the environment to point of exposure; population location and activities; time variation of release.
4. Food Samples	Concentrations of contaminants in food supply.	FDA Total Diet Study Program,[2] market basket studies, shelf studies.	Dietary habits of various age/sex/cultural groups. Relationship between food items sampled and particular (geographic, ethic, demographic) groups studied; relationships between concentrations in uncooked vs. prepared food.
5. Drinking Water Samples	Drinking water supply	Ground Water Supply Survey,[3] Community Water Supply Survey,[4] tap water.	Fate and distribution of pollutant from point of sample to point of consumption. Population served by specific facilities and consumption rates. For exposure due to other uses, e.g., cooking and showering, need to know activity patterns and volatilization rates.
6. Consumer Products	Concentration levels of various products.	Shelf surveys, e.g., solvent concentration in household cleaners [5].	Establish use patterns and/or market share of particular product, individual exposure at various usage levels, extent of passive exposure.
7. Breathing Zone Measurements (Industrial Studies).	Exposure to chemicals in an industrial setting.	Industrial hygiene studies, occupational surveys.	Fate of pollutants between monitoring and point of exposures, location, activities, time spent relative to monitoring locations. Protective measures/avoidance.
8. Microenvironmental Studies.	Ambient medium in a defined area, e.g., kitchen, automobile interior, office setting, parking lot.	Special studies of indoor air, radon measurements, office building studies.	Activities of study populations relative to monitoring locations and time exposed.
9. Surface soil sample	Soil available for contact	Soil samples at contaminated sites.	Fate of pollution on/in soil; activities of potentially exposed populations.
10. Soil Core	Soil including pollution available for ground water contamination; can be an indication of quality and trends over time.	Soil sampling at hazardous waste sites.	Fate of substance in soil, speciation and bioavailability, and contact and ingestion rates as a function of activity patterns and age.
11. Fish Tissue	Extent of insult to ecological population, and/or extent of contamination of edible fish tissue.	National Shellfish Survey,[6] special studies on local fish populations.	For ecological assessments: Relationship of samples to fish population (then see reconstructive assessment below). For humans: relationship of samples to food supply for individuals or population of interest, consumption habits, preparation habits.
B. *Direct Assessments:*			
1. Air Pump/Particulates and Vapors ("split sample" air).	Exposure of an individual or population via the air medium.	TEAM study,[7] carbon monoxide study [8].	Direct measure of individual exposure during time sampled; to characterize exposure to population, relationship between individuals and population must be established as well as relationships between times sampled and other times for the same individuals, and relations between sampled individuals and other populations. In order to make these links, activities of the sampled individuals compared to populations characterized are needed in some.

TABLE 3-1.—EXAMPLES OF TYPES OF MEASUREMENTS TO CHARACTERIZE EXPOSURE-RELATED MEDIA AND PARAMETERS—Continued

Type of measurement (sample)	Usually attempts to characterize (whole)	Examples	Typical information needed to characterize exposure
2. Split Sample Food/Split Sample Drinking Water.	Exposures of an individual or population via ingestion.	TEAM study [7]	Same as above.
3. Skin Patch Samples	Dermal exposure of an individual or population.	Pesticide Applicator Survey [9]	Same as above, skin penetration.
C. *Reconstructive Assessments:*			
1. Breath	Total absorbed dose for individuals or population (usually indicative of relatively recent exposures).	Measurement of VOCs, alcohol (usually limited to volatile compounds).	(1) Relationship between individuals and population; exposure history (i.e., steady-state or not) pharmacokinetics (chemical half-life), possible storage reservoirs within the body. (2) Relationship between breath content and body burden.
2. Blood	Total absorbed dose for individuals or population (usually indicative of relatively recent exposures).	Lead studies, pesticides, heavy metals (usually best for soluble compounds, although blood lipid analysis may reveal lipophilic compounds).	(1) Same as above. (2) Relationship between blood content and body burden.
3. Adipose	Total absorbed dose for individuals or population (usually indicative of long-term averages).	NHATS,[10] dioxin studies, PCBs (usually limited to lipophilic compounds).	(1) Same as above. (2) Relationship between adipose content and body burden.
4. Nails, Hair	Total absorbed dose for individuals or population (usually indicative of past exposure in weeks to months range; can sometimes be used to evaluate exposure patterns).	Heavy metals studies (usually limited to metals).	(1) Same as above. (2) Relationship between nails, hair content, and body burden.
5. Urine	Total absorbed dose for individuals or population (usually indicative of elimination rates), may vary in time since exposure depending on chemical.	PERC study,[11] TCE study [12]	(1) Same as above. (2) Relationship between urine content and body burden.

[1] U.S. EPA (1985b).
[2] U.S. EPA (1986b).
[3] U.S. EPA (1985b).
[4] U.S. EPA (1985e).
[5] U.S. EPA (1985d).
[6] U.S. EPA (1986b).
[7] U.S. EPA (1987a).
[8] U.S. EPA (1987a).
[9] U.S. EPA (1987d).
[10] U.S. EPA (1986e).
[11] U.S. EPA (1986d).
[12] U.S. EPA (1987e).

For example, if a chemical shows adverse effects through inhalation, but ingestion and dermal studies show no adverse effects, measurement data to characterize ingestion and dermal routes of exposure may be irrelevant.[2] Likewise, for a substance that shows adverse effects for some forms (vapor, solid, particular valence state, etc.) but not others, the assessor must evaluate and explain why the data used match with the chemical species of concern.

In addition to the general discussion of relevance above, the following sections deal with more specific issues of relevance.

3.2.1. Direct Measurement of Exposure

Direct exposure assessments always rely on measurements. Assessments using the direct measurement approach can be assessing individual exposures, exposures to groups of individuals or segements of a population (i.e., a subpopulation) of which the sampled individuals are a part. Each of these objectives of the overall exposure assessment presents different issues of relevance to using the data.

Data collected for the direct measurement approach are typically personal samples of an individual or small population sample. The data are usually chemical-specific, although samples of radiation, particulates, fibers, or other non-chemical-specific agents have been measured. The data are usually time-specific, and can be expressed in terms of a time-weighted average (TWA) (i.e., 1-hour TWA, 8-hour TWA, etc.) or a continuous curve (e.g., by using the recording carbon monoxide monitor). The data are usually location-specific, the location being wherever the individual with the personal monitor was during the period of measurement. It should be noted here that unless detailed records are kept of where the individual goes and for how long, this information may not be available to the assessor. The data are also usually a function of the specific activities of the individual during the period of measurement; this information is rarely available to the assessor in more than very broad categories, if at all.

To make the case that the direct measurement data are relevant to the exposure assessment being done, the exposure assessor must show that these factors for the data match the objective of the assessment. If there is an unknown or partial match between the data factors and the assessment objectives, the assessor must make, state, and justify assumptions that will establish a logical link. For example, if 8-hour TWA data are available, and the objectives of the assessment are to evaluate average exposure over 10 years, the 8-hour TWA data might be used if it is known (from other data, observation, etc.) that the concentrations/exposures do not vary significantly from day to day, and that

[2] A caution here; unless pharmacokinetics are reasonably well known and mechanisms of action identified, it is often very difficult to dismiss exposure routes as totally irrelevant, even if some studies show no apparent adverse effect.

the day selected for measurement is representative or typical (based on statistical considerations, etc.).

For those individuals for whom direct measurements of exposure have been made, these data may be used directly in individual exposure assessments provided the data are of adequate quality (see section 3.3), are measures of the appropriate chemical or agent, and are actually measuring exposure while it takes place. This is an unusual case in that it is one of the few times where measurement data may be used directly as exposure data. Individual direct measurement exposure assessments are usually done for the purposes of protecting the individuals, often in an occupational environment. When exposures are being compared to an action level, concern level, standard, or other benchmark, and the data are being taken to answer a yes/no question about whether exposure is above the benchmark, direct measurements properly collected are the most relevant data.

Direct measurement data are also used to characterize the exposures of a population, or a segment of a population, by making inferences from the individuals sampled to the population or population subgroup. The logical link between the individuals sampled and the entire population is considerably strengthened by statistics. If the individuals sampled were selected randomly, probabilistically, or in a manner that can be described with statistics, this link can perhaps be described quantitatively, and the exposure assessor is advised to consult a statistician to help in establishing the relevance of the data taken for individuals to the exposures of a population. It must be kept in mind that the population being characterized by the data is not necessarily the population desired for the objectives of the assessment, since the assessment may involve different times (summer, winter, etc.), different locations (all service station attendants vs. data taken for attendants in Cleveland, etc.), or different activity patterns (persons who eat fish vs. persons who do not eat fish, etc.). All of these differences between the data measured and the population for which the assessment requires characterization must be identified and logical links must be drawn between individual measurement data and population exposures before the data can be fully relevant.

3.2.2. Reconstructive Exposure Assessment

Measurement data for reconstructive exposure assessments are usually from individuals (although composite tissue samples from several individuals are sometimes used), are usually chemical-specific, and may also be location-specific, time-specific, and activity-specific. Some reconstructive exposure assessment samples will reflect exposures over the relatively recent past (e.g., exposures can be reflected in breath, blood, urine, and fecal samples after minutes-to-days), while others will be indications of exposures over a longer period of time (e.g., adipose tissue, bone, and hair samples are usually reflective of exposures that took place weeks-to-years previously). The key to linking measurements of body burden or other biomarkers to exposure assessment is pharmacokinetics (i.e., the time-dependent distribution, metabolism, transport, storage, and elimination of the agent within the organism). In addition, before these measurements can be used to reconstruct absorbed dose or exposure, information must be known on the properties of the chemical, individual characteristics (size, body fat content, etc.), and whether the exposure has been long-term, acute, intermittent, a past episode, etc.

Pharmacokinetics can also be used to establish the relevance of particular samples to the exposure assessment being considered. Because pharmacokinetics maps out where a substance is likely to go within an organism, it will indicate the relevance of various tissues or fluids as an indication of exposure. For example, for a lipid-soluble substance with a long half-life within the body (such as 2,3,7,8-TCDD), pharmacokinetic considerations would show that adipose tissue or blood fat samples may be very relevant while breath samples are irrelevant, since inside the body the chemical avoids the blood/breath elimination route and instead is stored in fat tissue.

As with the direct measurement data discussed in the preceding section, reconstructive exposure assessment usually use data from an individual, and so the inferences made from the samples will be to characterize the absorbed dose (or exposure if absorption data are available) for an individual. All of the considerations discussed previously about making inferences from individuals to populations also apply here.

3.2.3. Predictive Exposure Assessment

Use of measurement data in predictive exposure assessments can vary widely, from a speculative assessment where no measurements are used directly, to an assessment where extensive measurement data are used both to characterize the chemical and to characterize the activities of the individuals or populations assessed. Exposure assessments that use no measurement data directly have legitimate purposes in a regulatory agency, for example, where the chemical has not been manufactured yet so no measurements can be made, or in preliminary evaluations of exposure where great precision is not required.[3] However, most predictive exposure assessments use at least some measurement data.

Like the other approaches to exposure assessment, the predictive approach requires the assessor to make a logical link between the measurement data and the exposure. Because of the many different types of measurements used in predictive exposure assessment, making these links (say, from source measurements to exposures) can be complex. Using measurement data to quantify exposure is usually done using any of several forms or derivatives of a general exposure equation.

Exposure, or the contract of an agent with the exchange boundaries of an organism (i.e., skin, lungs, digestive tract, etc.), can be mathematically defined as the amount of the agent available for absorption at the exchange boundaries. Over a period of interest, T, this can be described as:

$$E = \int_{t=0}^{T} I \, dt \qquad (3\text{–}1)$$

where E is the exposure, I is the intensity of contract, and t is time. The units of E are "amount," usually a mass of a chemical, but amount can also be in terms of fibers of asbestos, radiological amounts, etc. if the dose-response relationship for which the exposure and dose information being calculated are also in these terms. For the sake of simplicity, the discussion that follows will use units of mass for E. Note that I varies over time and may even be zero for part of the period of interest from t=0 to t=T. The units of I are mass/time.

The intensity of contact, I, is a function of C, the concentration of the pollutant in the medium contacting the organism, and CR is the contact rate or extent of contact:

$$I = (C)\,(CR) \qquad (3\text{–}2)$$

[3] For example, many times a decision is needed as to which chemical to study first, or even whether to continue to study a chemical. Often these decisions involve few resource consequences and great precision is not necessary. This is not to say, however, that important decisions with large resource implications should be made based on assessments using no measurements if measurement data may make a difference in the decision.

The units of C and CR may vary, but must be compatible with each other and must lead to units of mass/time exposed for I. For example, if C is in units of M/M (e.g., mg/kg food ingested), CR is in units of M/T (e.g., kg food ingested/day). If C is in units of M/V (e.g., mg/L water ingested), CR is in units of V/T (e.g., L water ingested/day). Conversion factors may be necessary in assessing I. For example, if C is in units of V/V (e.g., ppm in air), a conversion factor to M/V (say, mg/m³ of air) would be necessary if CR is in the typical units of V/T (m³/day). For dermal exposures, if C is in units of, say, M/V of bulk material (e.g., mg/L), a conversion factor of the form (M/A)/(M/V) (say, mg available per cm² skin exposed/mg per L bulk material) yielding C in units of M/A (e.g., mg/cm²) with CR typically in A/T units (e.g., cm² skin exposed/hour).

The discrete form of equation 3–1 is:

$$E = \frac{\overset{N}{S}}{\underset{i=1}{}} I_i t_i = I_1 t_1 + I_2 t_2 + \ldots + I_n t_n \qquad (3\text{–}3)$$

where t_i now becomes the duration of exposure of event i, and I_i is the intensity of contact for exposure event i. For multiple exposure events over period of interest T (using equations 3–2 and 3–3):

$$E = \frac{\overset{N}{S}}{\underset{i=1}{}} I_i t_i = \frac{\overset{N}{S}}{\underset{i=1}{}} (C_i)(CR_i)t_i \qquad (3\text{–}4)$$

where

$$T = \frac{\overset{N}{S}}{\underset{1=1}{}} t_i \qquad (3\text{–}5)$$

for all events, and

$$ED = \frac{\overset{N}{S}}{\underset{i=1}{}} t_i \qquad (3\text{–}6)$$

for events where I is not zero. ED is the duration of exposure over all events where exposure occurs, that is, where the intensity of contact, I, is not zero.

The *exposure rate* can be defined as the exposure per unit of time. Certain average exposure rates can be useful in exposure assessment. Using equations 3–4 and 3–5, if $\bar{I}_c$ is a weighted average intensity of contact over the period of interest (including those segments of time when intensity is zero):

$ER_c = \bar{I}_c = E/T$ (3–7)

where ER_c is the calendar-time exposure rate. If equation 3–6 is used instead of 3–5, a similar exposure rate is derived for those times when exposure is actually occurring:

$ER_e = \bar{I}_e = E/ED$ (3–8)

Note that in equations 3–4, E is the same whether or not there are zero intensity terms on the right side of the equation, but 3–7 represents a calendar-time (or clock time) exposure rate and 3–8 represents and exposure-time exposure rate. The difference is whether the exposure rate, which is an average, is averaged over a period of time where sometimes exposure is zero, or is averaged over only those periods of time when exposure is occurring. By substitution,

$ER_c = I\ ED/T$ (3–9)

For cases where the contact rate, CR, is reasonably constant, and using the weighted average concentration for C, substituting equations 3–2 into 3–9 yields:

$ER_c = (C)\ (CR)\ (ED)/T$ (3–10)

where ER_c is the calendar-time exposure rate for period of interest T, and ED is the time during which exposure actually occurs at average concentration C and contact rate CR. This exposure rate can be normalized to unit body weight (BW) to yield a normalized calendar-time exposure rate. A commonly-encountered special case of this is the lifetime average daily exposure (LADE), where the period of interest is the lifetime (LT):

$LADE = (C)\ (CR)\ (ED)/(LT)\ (BW$ (3–11)

where, using representative units for water ingestion as an example:

LADE = lifetime average daily exposure [mg/kg/day]
C = average concentration [mg/L water ingested]
CR = contact rate [L water ingested/day]
ED = duration of time when exposure actually occurs days]
LT = lifetime [70 years converted to days]
BW = body weight (kg) (Note that this is average body weight over a lifetime and not merely the adult body weight.)

The resulting LADE is a normalized lifetime exposure rate. Another useful relationship encountered frequently is the dose equation, given in simplified form:

$D = (E)\ (AF)$ (3–12)

where D is dose (units are mass), E is exposure, and AF is an absorption fraction:

AF = amount absorbed/amount available for absorption (3–13)

These equations, when used with equation 3–11, give rise to another commonly encountered term, the lifetime average daily dose (LADD):

$LADD = (C)\ (CR)\ (ED)\ (AF)/(BW)\ (LT)$ (3–14)

Note that the concentration (C), the contact rate (CR), the exposure duration (ED), absorption fraction (AF), lifetime (LT), and body weight (BW) are all parameters that are specific to the individual, although the absorption fraction, body weight, and lifetime might usually be described with generic measurements, that is, averages for a population, since they are reasonably constant for an individual. Note also that both CR and ED are dependent on the activities of the individual, and the relevant data for these parameters are activity pattern data. A major task for the exposure assessor is to determine which measurement data are relevant to

determine C, the concentration of the agent that contacts the individual. In actual exposure situations, C is likely to vary over time, sometimes by a great deal.

There are several ways that exposure assessors use measurements such as those listed in Table 3–1 to determine C and to calculate exposures using the predictive approach. Three of these ways, each having a somewhat different approach to dealing with the variation in C (and other parameters), are the *scenario method,* the *microenvironment method,* and the *Monte Carlo method.* For all of these methods, the measurement data are first used to make inferences about environmental or ambient media, and how concentrations of the chemical or agent vary over time in those media. The logical links are formed and justified between the measurement (sample) data and the characterization of the media as given in the examples in Table 3–1. Once these characterizations are made, they are used to make inferences about exposure. These three methods are not mutually exclusive, and often are used in combination in exposure assessments.

The scenario method can be used either with a single scenario, usually starting with an average concentration to calculate an LADE or LADD as in equations 3–11 and 3–14, or with multiple scenarios. In the *single scenario method,* a set of assumptions is made about how exposure takes place for an individual, and values for the various parameters in the generic exposure equation are derived from the assumptions. For example, let us assume we are doing an exposure assessment concerned with chloroform in drinking water. Since it is known that chloroform may be formed as part of the chlorination process in a drinking water treatment plant, the drinking water treatment plant can be viewed as the source, and measurements can be made of the chloroform concentrations in the finished drinking water leaving the plant. Knowledge or data concerning the fate of chloroform in the distribution system will help build the logical link between the measurements at the treatment plant and later exposure; fate information may allow linking the concentrations at the plant with those at the tap.[4] An average concentration in tap water can be estimated from the data and fate considerations, say in this case, 20 mg chloroform/L tap water. Activity pattern data are used, or assumptions made, concerning the activities of the exposed individual, to determine what the parameters for contact rate and exposure duration will be for the scenario. For this scenario, assume the contact rate is two liters of tap water ingested daily, and that the individual lives at this location for 40 years (the exposure duration). Using a lifetime of 70 years (converted to days), and a body weight of 70 kg, the LADE calculation (using equation 3–11) is straightforward.

For the concentration parameter in the exposure equation, the single scenario method usually assumes it to be a single value. (The mean value and highest value reported are two common single-value treatments depending on whether the scenario is supposed to represent a "typical" or "worst case," respectively.[5] Recall that in the derivation of LADE in equation 3–11, it is an average intensity of contact for the exposure period. Substituting the highest value reported for the concentration term for a worst-case estimate in the LADE equation is essentially saying that the person will be exposed to that value on average for the duration of exposure (ED in equation 3–11). Variation in the concentration parameter C, as well as the other parameters, are often treated with ranges or a sensitivity analysis. Use of the single scenario method, where variation in the parameters is not used, can only be justified if individual exposures are being evaluated; applying a single scenario estimate to a population without considering variation is tantamount to saying all members of the population behave exactly the same way and are exposed to exactly the same concentrations of the chemical or agent. In cases where the variation is not known, single values may be used if explained in the uncertainty section of the assessment, where an analysis of the impacts of possible variation should be done.

A few words need to be said here about the use of "worst-case" scenarios. As discussed in Chapter 1, the exposure assessor is trying to estimate a real-world dose to use in the dose-response relationship for a risk assessment. By maximizing the parameters in a scenario for exposure, the assessor is looking at the top end of the distribution of exposures in a population (if indeed the worst case actually exists in the population). A legitimate use of worst-case scenarios is to determine if the exposure or risk is low enough even at this extreme so as to dismiss concern for this scenario. It is not legitimate to use a worst-case scenario to prove that there in fact exists a concern in a real population. In constructing a worst-case scenario, the assessor has usually added assumptions or used particular data points that bring into question whether the scenario actually represents the real world. If the exposure or risk value estimated by a worst-case scenario is high enough to cause concern, the assessor must reevaluate the parameters used and perform reality checks before deciding a problem really exists. It is critical that the results of a worst-case individual scenario are not immediately applied to an entire population, since in almost all cases this will result in a substantial overestimate of a potential problem.

In the *multiple scenario method,* several individual scenarios are constructed, with particular attention given to highlighting the variability of the parameters used for the scenarios. The most common use of multiple scenarios will be where a typical case and a worst case (or reasonable worst case) are constructed, using the same procedures described above. In its theoretical extreme, one could construct a different scenario for each individual, using the particular values of the parameters which apply to that individual, and derive an estimate of population exposures by aggregating the individual scenarios.[6] With populations

[4] Alternately, of course, one could take measurements at the tap and consider that as the source for the purpose of the assessment. Where this approach may cut down uncertainty for the individual exposure, it makes generalization to a population from the individual estimates somewhat more difficult since the relationship among the individuals as far as differences in concentration at the tap is unknown.

[5] A worst-case scenario is one that estimates the highest exposure. One form of worst-case scenario is the so-called "maximally exposed individual" (MEI), which represents the single individual with the highest exposure. Naturally, the worst case can be arrived at in a number of ways besides maximizing concentration; the exposure can often be much more sensitive to the activities of the individual (ingestion rates, for example). In most exposure assessments, adjusting all the parameters to their limiting values would maximize exposure results in a scenario that may not have realistic chance of happening in the real world. For example, in the drinking water scenario, maximizing all parameters in an LADD calculation would mean the individual with the smallest body weight and shortest lifetime consumed the most water per day at the highest concentration for the longest duration; this combination is unlikely to actually occur since at least some of the parameters (e.g., body weight and consumption rate) may be covariant. For this reason, the concept of "reasonable worst-case" scenarios is often used, where the exposures are high but the combination of parameters thought to be one which probably occurs in the actual population.

[6] This has in fact been done by the Office of Toxic Substances for the 4920 respondents in the OTS chlorinated solvents study, as reported in the Task #43 report to contract 68–02–4254, dated 8/31/87, titled, "Consumer Exposure Estimates for Solvents."

of more than a small number of individuals, this may become unwieldy, but often groups of individuals will be treated as behaving similarly enough to be covered by a single scenario, thereby dividing the population into subpopulations. This procedure is often done when estimating occupational exposures for a single chemical across a number of job types. Each job type is covered by a different scenario which uses the particular parameters pertinent to that job.

The *microenvironment method* treats the variability in the concentration contacted, C, as a series of constants. If the contact rate is assumed to be fairly constant during periods of exposure, equation 3–4 can be reduced to:

$$E=(CR)\sum_{i=1}^{N} C_i, \qquad (3\text{–}15)$$

where each microenvironment i has associated with it a characteristic concentration C_i, and the subject spends a duration t_i in that microenvironment. In this method, the individual's surroundings are divided into compartments where the chemical or agent concentration remains constant, or at least has a known and describable variability. Measurement data for concentrations of chemicals or agents are usually described as constants (usually means of the measured data) for each microenvironment. Exposure estimates are derived by using an exposure equation such as the one described above, evaluating each microenvironment, and summing over all the microenvironments for an individual. Unlike the scenario methods described in equation 3–11, however, which essentially evaluate average individual exposure and which can then be aggregated to populations, the microenvironment method can more easily directly incorporate data on population activity patterns into the estimate by assigning statistical weights to the various microenvironments.

The *Monte Carlo method* immediately uses the fact that the parameters in the generic exposure equation are not single values, but distributions of values, to derive a distribution of exposures in the population. Using computer-assisted iterative techniques, the Monte Carlo simulation will solve exposure equations multiple times (hundreds, thousands) using all the actual values observed from measurements or characterization of the media, and all the data about activity patterns. The technique involves using random combinations of the actual data enough times to generate a distribution of estimated exposures while recreating the distribution of the data on the equation parameters. Although this may superficially resemble the theoretical extreme of the multiple scenario method discussed previously, it is fundamentally different, since the multiple scenario method purposefully combines the values from the distribution and the Monte Carlo method does this randomly. Whereas the multiple scenario technique may be impracticable if the population is large, the Monte Carlo method is not limited by a large population. Because of the way the estimate is derived, however, the Monte Carlo method has several issues that the exposure assessor must keep in mind before using it. First, the Monte Carlo technique works on the assumption that the parameters are independent; if they are not independent, but assumed so, excessive error may result. There are methods, however, to account for covariance if known. Second, and a more resource-related concern for most exposure assessors, is that the variation or distribution of the input parameters must be known. For the assessor using measurement data to derive distributions of concentrations or activities, this may have important ramifications to the sampling plan, and it is best to consult a statistician about the possibility of using the data for Monte Carlo simulations before the date are collected.

3.2.4. Measurements and Modeling

In exposure assessments, exposure models based on mathematical equations are used extensively to calculate things such as environmental fate/transport in surface water, indoor air levels of chemicals volatilizing from consumer products, etc. These exposure models and exposure-related measurements should be mutually supportive. When an analytical method for a particular chemical and medium is well established, and models are just being developed, all collected measurement data can be used to validate the models. Conversely, when such an analytical method is being developed and the appropriate mathematical models are well accepted, the models can be part of the process of verifying the data from the analytical method. Whenever the relative certainty of models and the relevant measurements of adequate quality are in question, the assessor should favor the measurements.

EPA's Office of Research and Development is in the process of establishing criteria for the selection of exposure assessment-related models that are most useful for a particular scenario. Part of this process involves the use of measurement data to answer selection criteria questions (e.g., fate and transport, degradation rates). Model selection criteria documents already exist for ground water (U.S. EPA, 1988d) and surface water (U.S. EPA, 1987c) and are being developed for other media.

Monitoring data and environmental fate modeling are complementary tools used to help estimate exposure. A combination of monitoring data and estimates obtained from environmental modeling reduces uncertainty in estimating chemical concentrations at exposure points. While monitoring data have the advantage of being actual measurements at the pollution site, they may have potential limitations, particularly in assessing long-term trends. However, measurement data, which are autocorrelated, can be used to predict trends in future exposures (Roach, 1977). Over-reliance on monitoring data can cause underemphasis of chemicals that have not yet been released from a source or are slow moving.

Another question related to monitoring data, which modeling helps resolve, is whether they are representative only of their sampling locations, or are relevant also to an overall exposure assessment. Because chemical concentrations are spatially variable, the assessor may need to use modeling for proper spatial representativeness in the exposure assessment. Monitoring usually represents a spatial distribution that is by necessity limited. The use of models in conjunction with monitoring can project chemical concentrations over space and time, thereby strengthening the logical link between measurement data and exposures.

3.2.5. Use of Surrogate Data in Pesticide Exposure Assessment

The use of surrogate data plays a major role in EPA assessments of human non-dietary exposure to chemicals, especially in the Office of Pesticide Programs. According to the Agency's "Pesticide Assessment Guidelines, Subdivision U, Applicator Exposure Monitoring" (U.S. EPA, 1987d): "Surrogate exposure data are defined as exposure monitoring data collected for other pesticide chemicals using comparable methods and under similar conditions as for the pesticide under assessment." The mechanics of the use of surrogate data have been discussed in public fora and in the published

scientific literature in recent years. The assumption in the use of surrogate data is that in many pesticide application scenarios, the physical parameters of application (such as human activity which leads to exposure), not the properties of the pesticide, are most important in determining the level of exposure. Note that when using a passive dosimetry monitoring method, what is measured is the amount of chemical impinging on the skin surface, or available for inhalation, that is, exposure, not the actual dose received. Factors such as dermal penetration, are, of course, expected to be highly chemical-dependent.

The development of a surrogate data base, and valid predictive correlations where possible, is a procedure that the Agency will continue to pursue. The Agency believes that it is more reliable to estimate exposure based on an extensive, scientifically sound and appropriate "surrogate" data base rather than on the results of an individual pesticide application study with a limited number of replicates, even if that single study is judged valid by the Agency. As the Agency receives additional valid exposure data from any source, the data will be added to the existing data base, thus expanding the data base and improving its reliability for estimating exposure for other pesticides.

3.2.6. Combining Measurement Data Sets from Various Studies

Combining data from more than one source into a single data set must be done cautiously. The circumstances under which each set of data was collected (target population, sampling design, location, time, etc.) and the quality of the data (precision, accuracy, representativeness, completeness, etc.) must be evaluated. Combining summary statistics of the data sets (e.g., means) into a single data set may be more appropriate than combining the original data values. Statistical methods are available for combining results from individual statistical tests. For example, in applicable cases, several studies with marginally statistically significant results may justify an overall conclusion of a statistically significant effect.

The best way to report data is to provide sufficient background information for the measurement data set, including clear documentation of the source of the data (including references). This allows for determining the underlying probability distribution of the measurement variable. A probability distribution can be ascertained from the following types of information about the data set: the arithmetic or geometric mean, the number of measurements in the data set, the extreme values, the mode or modes, the median value, the variance or standard deviation, and a histogram showing the general shape of the distribution.

Arithmetic means are good descriptors of the central tendency of a data set provided the data set is normally distributed. Geometric means are better descriptors of central tendency for lognormal distributions. The median is a good measure of the location of the center of a data set because it is unaffected by extreme values. Unfortunately, it does not make use of all the information contained in the data set, but rather uses only the relative sizes of the measurements. The median is also less amenable than a mean to mathematical treatment, and is more difficult to use in more elaborate statistical techniques.

3.3. *Adequacy of Measurement Data for the Intended Exposure Assessment*

Measurement data, whether generated for the particular exposure assessment or taken from another measurement study, must be evaluated for their adequacy in use as samples representative of media, individual exposures, body burden, or whatever is being characterized. The same considerations discussed in section 2.4 concerning data quality (precision, accuracy, representativeness, completeness, and comparability) are appropriate when evaluating any data being considered for use in an assessment.

Even in the case of serious flaws, data should not be discarded entirely unless better data are available. If flawed data are retained, the nature and seriousness of the flaws should be clearly stated. If flawed data are rejected for use in exposure assessments in favor of better data, the flaws should be clearly stated and the basis for judgment of the retained data should be documented.

3.3.1. Quality Assurance and Quality Control for Previously-Generated Data

In many instances, previous studies may have developed data that could be useful for the current sampling plan requirements of the exposure assessor. Any data developed through previous studies should be validated with respect to quality and extrapolation to current use. The criteria for method selection and validation should also be followed in the analysis of existing data. Some other considerations when evaluating data include the following:

Analytical Methods—Were the analytical methods used in collecting or analyzing the data from the previous study consistent with present practices? The methods need not be identical, and a lower detection limit with a newer method does not necessarily mean that the older data are inadequate. However, research might have identified problems with older methods that would invalidate them for current use.

Detection Limits—It should be determined whether the detection limits of the analytical method were sensitive to current Agency standards and criteria for evaluating data.

Laboratory—Was the laboratory performing the analysis considered competent? Are matrix spike recoveries acceptable for the intended use? Were any laboratory blanks contaminated?

Sample Collection Considerations—Was the sampling plan followed? Where and how were the samples collected? Were a sufficient number of samples collected? Methods for sample collection are as important as methods for sample analysis.

Sample Handling Considerations—Were traceability procedures followed if the samples were analyzed off-site? Were the samples preserved properly? How were the samples shipped? How long were the samples held before being analyzed?

3.3.2. The Role of Limit of Detection (LOD) Values in Measurements Used to Estimate Exposure

The ability to detect and accurately measure a quantity tends to decrease at low concentrations due to various factors such as sampling constraints, limitations of the measuring instrument, contamination from sources other than the source being considered, etc. The limitations of the measuring system must be understood when interpreting data for exposure assessment.

The limit of detection (LOD) is the smallest concentration or amount of a substance that can be reliably detected by a given measurement process. The limit of quantitation (LOQ) is the smallest concentration or amount of a substance for which quantitative results may be obtained with a specified degree of confidence. The precise interpretation of these definitions depends on the analytical method (e.g., particle counting methods differ from methods such as GC–MS with essentially continuous results) and the substance being analyzed. The definitions tend to vary also between applications and laboratories ("reliably detected" may be defined as detected with a probability of 95%, 99%, 99.9%, etc.).

The exposure assessor should ensure that the LOD and LOQ have been clearly defined and estimated for the

measurement process under consideration and are appropriate for the needs of the exposure assessment. The laboratory should not only state numerical values, but definitions of the LOD and LOQ.

Exposure assessors may often be faced with data consisting largely of "below LOD" or "at LOD" values. Since the exposure assessment is only as good as the data supporting it, it is essential to interpret these types of data properly so as to avoid misrepresenting the data set or the exposure assessment itself. Rules of thumb that the exposure assessor may encounter in the way data sets are reported include:

Data less than the LOD reported as "non-detected"—When measurements less than the LOD are reported as non-detected, the data are referred to as censored. The level of censoring is based on the confidence with which the analytical signal can be discerned from the noise. Statistical methods are available for treating these data sets and many are summarized and include working examples (Cox and Oakes, 1984; Miller, 1981; Kalbfleisch and Prentice, 1980; Porter et al., 1988).

All Non-detects reported as LODs—In this worst-case approach, all non-detects are assigned the value of the LOD, which may be considered the largest concentration of analyte that could be present but not yet detected. This approach biases the mean in a positive direction. The seriousness of such a bias will depend on the relative number of detects and non-detects in the data set and the relative size of the detection limit compared to the mean of the data with values above the LOD.

All non-detects reported as zero—This approach results in biasing the mean in a negative direction. Again, the seriousness of the bias depends on the relative number of detects and non-detects and the mean of the data with values above zero.

All non-detects as LOD/2—This approach assumes that on the average all values between the LOD and zero could be present; therefore, an average value would result if many samples in this range were measured. Similar to the above approaches, the seriousness of the bias depends on the relative number of detects and non-detects and the mean of the data above LOD/2.

Another option includes all measured values reported, without regard to the considerations for LODs and LOQs. Negative values (e.g., a blank larger than the value measured for a sample) must be reported when they occur. Indeed, if a population value is truly zero, an equal number of negative and positive measured values is expected because of the measurement variability. Using this approach, the mean and standard deviation of the data set are the important parameters, and the results for individual samples should not be considered apart from the data set.

3.4. *Evaluation and Description of Uncertainty in the Use of Measurements*

The estimation of a quantitative value of a parameter using measurement data is an inexact process. Every measurement results in a somewhat different value for the parameter. Thus, the resulting data and any decisions based on them have a degree of *measurement uncertainty*. When using field or laboratory measurement in the decision-making process, the exposure assessor must always evaluate the data for their uncertainty and assess them for the error associated with the risk estimate. The assessment will also contain *descriptive uncertainty*, which refers to the uncertainty in the logic of how the measured data and the exposures are linked. Descriptive uncertainty as well as measurement uncertainty must be clearly indicated in the assessment. An error in descriptive logic about how the measurements and the exposures are linked may mean the difference between estimating exposures that do or do not actually occur in the real world, with resulting health, ecological, or economic consequences. For that reason, it is essential that the non-numeric assumptions about how the measurements and exposures are linked are clearly laid out in the uncertainty analysis.

Most predictive or reconstructive exposure assessments, and often direct measurement assessments, also rely somewhat on expert judgment. Section 3.4.3 discusses formal means for representing uncertainty due to expert opinion.

3.4.1. Assignment of Limits of Uncertainty to Data

Any assignment of uncertainty to data must consider both random and systematic sources of error and, for the measurement process, the sampling operation and the relation of the samples to the population of concern. The assignment of measurement uncertainty must be made on the basis of a statistical analysis of the data. However, even the best statistical treatment may often involve some subjective decisions. Accordingly, all details of the analysis of the data must be documented, and clear statements must be made as to what the assigned uncertainties represent.

3.4.2. Statistical Analysis of Data

The services of a professional statistician are essential in the exposure assessment process when data are being analyzed statistically.

The evaluation of both the mean and the dispersion of a data set depends on the knowledge or assumption of the type of distribution of the population. Types range from a uniform distribution in which all individuals have the same frequency of occurrence (e.g., flipping a coin) to those in which the frequencies of occurrence vary and may be symmetrically or asymmetrically distributed. The normal distribution is the type most frequently encountered and is familiar to most scientists. The results of measurement processes are often normally distributed. Individual samples from environmental media often exhibit a log-normal distribution. Log-normal data can be transformed to normal data by first converting to logarithms and then treating the logarithms as if they were the actual data. It would be useful to graph the available data to ensure that the results are normally distributed. There are computerized statistics packages on the commercial market that facilitate the determination of data distribution. Also, a limited number of samples may preclude statistical analysis of the data.

Depending on the distribution of data, statistics such as dispersion, range, standard deviation, and confidence intervals can be developed, as well as measures of bias and uncertainty. Again, the exposure assessor is advised to consult a statistician or good statistics text for further information and guidance in this area.

3.4.3. Decision Analytic Approach for Expert Opinion

The decision analytic approach explicitly characterizes and represents major uncertainties using probability as the language to convey the degree of uncertainty. When the available data are too indirect, conflicting, or incomplete to draw relationships of concern, the National Academy of Sciences, in its 1977 review of EPA's decision-making procedures, endorsed the use of (judgmental) probabilities as a means for scientific experts to communicate more precisely their knowledge concerning scientific uncertainties to decision-makers (National Academy of Sciences, 1977). An important issue in implementing a decision analytic assessment is the selection of the exposure experts to provide probabilistic exposure relationships. There is extensive

literature covering techniques used for eliciting probability judgments from experts and the various types of bias that can occur when experts make such judgments (Von Holstein and Matheson, 1979; Spetzler and Von Holstein, 1975; Kahneman et al., 1982; Wallsten and Budescu, 1983).

Bayesian inference is worthy of note for combining expert opinion and experimental or survey data. This approach to representing uncertainty is to begin with a prior probabilistic distribution to represent the uncertainty, based on expert opinion, anecdotal information interpreted by an expert, or other sources. The prior distribution is then updated using experimental data and standard Bayesian statistics to obtain an updated or "posterior" distribution, which is taken to be the final form of the distribution (see Hayes et al., 1987, or any statistics text covering Bayesian inference).

Glossary of Terms

Absorbed Dose—The amount of a substance penetrating across the exchange boundaries of an organism, via either physical or biological processes, after contact (exposure).

Accuracy—The measure of the correctness of data, as given by the difference between the measured value and the true or standard value.

Administered Dose—The amount of a substance given to a human or test animal in determining dose-response relationships, especially through ingestion or inhalation. (See applied dose.) Even though this term is frequently encountered in the literature, administered dose is actually a measure of exposure, because even though the substance is "inside" the organism once ingested or inhaled, administered dose does not account for absorption. (See absorbed dose.)

Agent—A chemical, radiological, mineralogical, or biological entity that may cause deleterious effects in an organism after the organism is exposed to it.

Ambient—Surrounding conditions. "Indoor ambient" and "outdoor ambient" are sometimes used to differentiate between indoor and outdoor surroundings.

Ambient Measurement—A measurement (usually the concentration of a chemical or pollutant) taken in an ambient medium, normally with the intent of relating the measured value to the exposure of an organism which contacts that medium.

Ambient Medium—One of the basic categories of material surrounding or contacting an organism, e.g., outdoor air, indoor air, water, or soil, through which chemicals or pollutants can move and reach the organism. (See biological medium, environmental medium.)

Applied Dose—The amount of a substance given to a human or test animal in determining dose-response relationships, especially through dermal contact. (See administered dose.) Even though this term is encountered in the literature, applied dose is actually a measure of exposure, since it does not take absorption into account.

Arithmetic Mean—The sum of all the measurements in a data set divided by the number of measurements in the data set.

Breathing Zone—A zone of air in the vicinity of an organism from which respired air is drawn. Breathing zone measurements are frequently made in occupational health studies by placing monitors at fixed locations of approximately head height near where a worker spends a substantial amount of the workday.

Bias—A systematic error inherent in a method or caused by some feature of the measurement system.

Biological Measurement—For the purposes of reconstructive exposure assessment, a measurement taken in biological medium, usually of the concentration of a chemical/metabolite or the status of a biomarker, normally with the intent of relating the measured value to the absorbed dose of a chemical at some time in the past. (Biological measurements are also taken for purposes of monitoring health status and predicting effects of exposure.) (See ambient measurement.)

Biological Medium—One of the major categories of material within an organism, e.g., blood, adipose tissue, or breath, through which chemicals can move, be stored, or be biologically, physically, or chemically transformed. (See ambient medium, environmental medium.)

Comparability—The ability to describe likenesses and differences in the quality and relevance of two or more data sets.

Data Quality Objectives (DQO)—Statements of the level of uncertainty an assessor is willing to accept in results derived from environmental data.

Direct Measurement of Exposure—An approach to quantifying exposure by taking measurements of exposure at or near the exchange boundaries of an organism while the exposure is taking place.

Dose—The amount of a substance available for interaction with metabolic processes of an organism following exposure and absorption into the organism. The amount of a substance crossing the exchange boundaries of skin, lungs, or digestive tract is termed *absorbed dose*, while the amount available for interaction by any particular organ or cell is termed the *delivered dose* for that organ or cell. Theoretically, the sum of the delivered doses plus the metabolic transformations should equal absorbed dose. (The terms *adminstered dose* and *applied dose* refer to amounts of a substance made available for absorption, and therefore are measures of exposure rather than dose. As such, these terms, sometimes found in the literature, are somewhat confusing and should be avoided if possible by exposure assessors. The term *exposure dose*, a common radiological term, refers to exposure but carries the assumption that the absorption fraction is one, making exposure equal to absorbed dose. Again, this term is somewhat confusing and should be avoided if possible.)

Dose Rate—Dose per unit time, for example in mg/day. Dose rates are often normalized to body weight, yielding units such as mg/kg/day.

Dose-Response Assessment—The determination of the relationship between the magnitude of exposure and the probability of occurrence of the health effects in question.

Dose-Response Curve—A representation, normally in a graphical presentation, of the relationship between dose and probability of occurrence of a health effect or effects. Often these curves are actually based on "administered dose" (i.e., exposure) rather than absorbed dose or delivered dose. (See discussion under "dose.")

Dosimeter—Instrument to measure dose; many so-called dosimeters actually measure exposure rather than dose.

Dosimetry—Process of measuring dose.

Ecological Exposure—Exposure of a nonhuman receptor or organism to a chemical, radiological, or biological agent.

Effluent—(Waste) material being discharged into the environment, either treated or untreated. Effluent generally is used to describe water discharges to the environment, although it can refer to stack emissions or other material flowing into the environment.

Environmental Fate—The destiny of a chemical or biological pollutant after release into the environment. Environmental fate involves temporal and spatial considerations of transport, transfer, storage, and transformation.

Environmental Fate Model—In the context of exposure assessment, any mathematical abstraction of a physical

system used to predict the concentration of specific chemicals as a function of space and time subject to transport, intermedia transfer, storage, and degradation in the environment.

Environmental Medium—One of the major categories of material found in the outdoor natural physical environment that surrounds or contacts organisms, e.g., surface water, ground water, soil, or air, and through which chemicals or pollutants can move and reach the organisms. (See ambient medium, biological medium.)

Exposure—Contact of an organism with a chemical, physical, or biological agent. Exposure is quantified as the amount of the agent available at the exchange boundaries of the organism (e.g., skin, lungs, digestive tract) and available for absorption.

Exposure Assessment—The determination or estimation (qualitative or quantitative) of the magnitude, frequency, duration, and route of exposure.

Exposure Pathway—The course a chemical or pollutant takes from the source to the organism exposed.

Exposure Rate—Exposure per unit time (compare exposure, dose, dose rate), yielding units of amount (mass, fibers, etc.)/time, for example, mg/day. Exposure rates are often normalized to body weight, yielding units such as mg/kg/day.

Exposure Route—The way a chemical or pollutant enters an organism after contact, e.g., by ingestion, inhalation, or dermal absorption.

Exposure Scenario—A set of assumptions about how exposure takes place (including assumptions/conditions concerning sources, exposure pathways, concentrations of pollutants, individual or population habits and characteristics), which aid the exposure assessor in evaluating, estimating, or quantifying exposures.

Fixed-Location Monitoring—Sampling of an environmental or ambient medium for pollutant concentration at one location continuously or repeatedly over some length of time.

Geometric Mean—The nth root of the product of n values.

Guidelines—Principles and procedures to set basic requirements for general limits of acceptability for assessments.

Hazard Identification—The determination of whether a particular substance or chemical is or is not causally linked to particular health effects.

Limit of Detection (LOD)—The smallest concentration or amount of a substance that can be differentiated from background by a given measurement process (e.g., analytical instrument/sample matrix combination). (See limit of quantitation.)

Limit of Quantitation (LOQ) (also, "limit of quantification")—The lower limit of concentration or amount of substance for which quantitative results may be obtained with a specified degree of confidence (i.e., the amount that must be present before a particular method is considered to provide reliable and reproducible quantitative results). (See limit of detection.)

Maximally Exposed Individual (MEI)—The single individual with the highest exposure in a given population.

Median Value—The value in a measurement data set such that half the measured values are greater and half are less.

Microenvironment Method—A method used in predictive exposure assessments to estimate exposures by sequentially assessing exposure for a series of areas (microenvironments) that can be approximated by constant or well-characterized concentrations of a chemical or other agent.

Microenvironments—Well-defined areas such as the home, office, automobile, kitchen, store, etc. that can be treated as homogeneous (or well characterized) in the concentrations of a chemical or other agent.

Mode—The value in the data set that occurs most frequently. Monte Carlo Method—A method used in predictive exposure assessments that uses the Monte Carlo technique, a repeated random sampling from the distribution of values for each of the parameters in a generic exposure equation, to derive an estimate of the distribution of exposures in the population.

Non-Parametric—Statistical methods that do not assume a particular statistical distribution for the statistical population(s) of interest ("distribution-free methods").

Personal Measurement—A measurement collected from an individual's immediate environment using direct methods such as personal air pumps.

Pharmacokinetics—The study of the time course of absorption, distribution, metabolism, and excretion of a foreign substance (e.g., a drug or pollutant) in an organism's body.

Precision—A measure of the reproducibility of a measured value under a given set of conditions.

Predictive Exposure Assessment—An approach to quantifying exposure by measurement or estimation of both the amount of a substance contacted, and the frequency/duration of contact, and subsequently linking these together to estimate exposure. Predictive exposure assessments commonly use the scenario method, the microenvironment method, or the Monte Carlo method (or combinations of these) to make the link between amount (intensity of contact) and duration of contact.

Probability Samples—Samples selected from a statistical population such that each sample has a known probability of being selected.

Quality Assessment—The overall system of activities that provide an objective measure of the quality of data produced.

Quality Assurance—The system of activities whose purpose is to provide to the user of the exposure assessment the assurance that the data used as a basis for the assessment meet defined standards of quality.

Quality Control—The overall system of activities whose purpose is to control the quality of the measurement data so that they meet the needs of the user.

Random Samples—Samples selected from a statistical population such that each sample has an equal probability of being selected.

Range—The difference between the largest and smallest values in a measurement data set.

Reconstructive Exposure Assessment—An approach to quantifying exposure by reconstructing absorbed dose (and exposure) after exposure has occurred, from evidence within an organism such as chemical levels in tissues or fluids, or from evidence of other biomarkers of exposure.

Representativeness—The degree to which a sample is, or samples are, characteristic of the whole medium, exposure, or dose for which the samples are being used to make inferences.

Risk—The probability of deleterious health or environmental effects.

Risk Characterization—The description of the nature and often the magnitude of human or non-human risk, including attendant uncertainty.

Sample—A small part of something designed to show the nature or quality of the whole. Exposure-related measurements are usually samples of environmental or ambient media, exposures of a small subset of a population for a short time, or biological samples, all for the purpose of inferring the nature and quality of parameters important to evaluating exposure.

Sampling Frequency—The time interval between the collection of successive samples.

Sampling Plan—A set of rules or procedures specifying how a sample is to be selected and handled.

Scenario Method—A method used in predictive exposure assessment to account for variability in exposure parameters by setting up one or more alternative sets of assumptions (scenarios), evaluating each for the resulting exposures, and then using the resulting exposure estimate(s) as being illustrative of the exposures in the actual populations being evaluated. In the case of a single scenario, a sensitivity analysis is usually performed on the parameters to evaluate the variability.

Source Characterization Measurements—Measurements made to characterize the rate of release of agents into the environment from a source of emission such as an incinerator, landfill, industrial or municipal facility, consumer product, etc.

Standard Operating Procedure (SOP)—A procedure adopted for repetitive use when performing a specific measurement or sampling operation.

Statistical Control—The process by which the variability of measurements or of data outputs of a system is controlled to the extent necessary to produce stable and reproducible results.

Statistical Significance—An inference that the probability is low that the observed difference in quantities being measured could be due to variability in the data rather than an actual difference in the quantities themselves. The inference that an observed difference is statistically significant is typically based on a test to reject one hypothesis and accept another.

Surrogate Data—Substitute data or measurements on one substance used to estimate corresponding values of another substance.

References

American Chemical Society (1983) Principles of environmental analysis. Anal. Chem. 55: 2210–2218.

American Chemical Society (1988) Principles of environmental sampling. ACS Professional Reference Book, Laurence H. Keith, ed. Washington, DC.

Cox, D.R.; Oakes, D. (1984) Analysis of survival data. New York, NY: Chapman and Hall.

Hayes, S.R.; Rosenbaum, A.S.; Wallsten, T.S.; Whitfield, R.G.; Winkler, R.L. (1987) Assessment of lung function and symptom health risks associated with attainment of alternative ozone NAAQS. Draft final report prepared by Systems Applications, Inc. for U.S. EPA Office of Air Quality Planning and Standards, Research Triangle Park, NC.

Kahneman, D.; Slovic, P.; Tversky, A. (1982) Judgment under uncertainty: heuristics and biases. Cambridge, England: Cambridge University Press.

Kalbfleisch, J.; Prentice, R.L. (1980) The statistical analysis of failure time data. New York, NY: Wiley.

Long, G.L.; Winefordner, J.D. (1983) Limit of detection: a closer look at the IUPAC definition. Anal. Chem. 55(7): 712A–724A.

National Academy of Sciences (1977) Decision making in the Environmental Protection Agency, volume 2. National Academy of Sciences, Washington, DC.

National Research Council (1983) Risk assessment in the federal government: managing the process. Washington, DC: National Academy Press.

Nelson, J.D.; Ward, R.C. (1981) Statistical considerations and sampling techniques for ground-water quality monitoring. Ground Water 19(6):617–625.

Porter, P.S.; Ward, R.C.; Bell, H.F. (1988) The detection limit. Environ. Sci. Technol. 2(8):856–861.

Roach, S.A. (1977) A most rational basis for air sampling programmes. Ann. Occup. Hyg. 20:65–84.

Sanders, T.G.; Adrian, D.D. (1978) Sampling frequency for river quality monitoring. Water Resources Research 14(4):569–576.

Schweitzer, G.E.; Black, S.C. (1985) Monitoring statistics. Environ. Sci. Technol. 19(11):1026–1030.

Schweitzer, G.E.; Santolucito, J.A. (1984) Environmental samplying for hazardous wastes. American Chemical Society Symposium Series Number 267. Washington, DC.

Shaw, R.W.; Smith, M.V.; Pour, R.J.J. (1984) The effect of sample frequency on aerosol mean-values. Air Pollution Control Association 34(8): 839–841.

Spetzler, C.S.; Von Holstein, C.A.S. (1975) Probability encoding in decision analysis. Manage. Sci. 22:340–358.

U.S. EPA. (1983) Interim guidelines and specifications for preparing quality assurance project plans. Office of Exploratory Research, Washington, DC. NTIS PB83–170514. [NTIS31191921].

U.S. EPA. (1984a) Study of carbon monoxie exposure on residents of Washington, D.C. and Denver, Colorado. Environmental Monitoring Systems Laboratory, Office of Research and Development, Research Triangle Park, NC. EPA–600/S4–84–031, NTIS PB84–183516.

U.S. EPA. (1984b) Soil sampling quality assurance user's guide. Environmental Monitoring Systems Laboratory, Office of Research and Development, Las Vegas, NV. EPA–600/4–84–043, NTIS PB84–198621.

U.S. EPA. (1984c) Survey management handbook. Vols. I and II. Office of Policy, Planning and Evaluation, Washington, DC. EPA–230/12–84/002.

U.S. EPA. (1985a) Methods for assessing exposure to chemical substances. Volume 1: Introduction. Office of Toxic Substances, Washington, DC. EPA–560/5–85–001, NTIS PB86–107083.

U.S. EPA. (1985b) Methods for assessing exposure to chemical substances. Volume 2: Methods for assessing exposure to chemicals in the ambient environment. Office of Toxic Substances, Washington DC. EPA–560/5–85–002, NTIS PB86–107067.

U.S. EPA. (1985c) Methods for assessing exposure to chemical substances. Volume 3: Methods for assessing exposure from disposal of chemical substances. Office of Toxic Substances, Washington, DC. EPA–560/5–85–003, NTIS PB86–107059.

U.S. EPA. (1985d) Methods for assessing exposure to chemical substances. Volume 4: Methods for enumerating and characterizing populations exposed to chemical substances. Office of Toxic Substances, Washington, DC. EPA–560/5–85/004, NTIS PB86–107042.

U.S. EPA. (1985e) Methods for assessing exposure to chemical substances. Volume 5: Methods for assessing exposure to chemical substances in drinking water. Office of Toxic Substances, Washington, DC. EPA–560/5–85/005, NTIS PB86–1232156.

U.S. EPA. (1985f) Methods for assessing exposure to chemical substances. Volume 6: Methods for assessing occupational exposure to chemical substances. Office of Toxic Substances, Washington, DC. EPA–560/5–85–006, NTIS PB86–157211.

U.S. EPA. (1985g) Methods for assessing exposure to chemical substances. Volume 9: Methods for assessing exposure to chemical substances resulting from transporation-related spills. Office of Toxic Substances, Washington DC. EPA–560/5–85–009.

U.S. EPA. (1985h) Practical guide for ground-water sampling. Robert S. Kerr Environmental Research Lab, Office of Research and Development, Ada, OK, EPA–600/2–85–104, NTIS PB86–137304.

U.S. EPA. (1985i) Sediment sampling quality assurance user's guide. Environmental Monitoring and Support Laboratory, Office of Research and Development, Las Vegas, NV, EPA–600/4–85–048, NTIS PB85–233542.

U.S. EPA. (1986a) Guidelines for estimating exposures. **Federal Register** 51:34042–34054.

U.S. EPA. (1986b) Methods for assessing exposure to chemical substances. Volume 8: Methods for assessing environmental pathways of food contamination. Office of Toxic Substances, Washington, DC. EPA–560/5–85–008.

U.S. EPA. (1986c) Handbook: Stream sampling for waste load allocations applications. U.S. Environmental Protection Agency, Cincinnati, OH. EPA–625/6–86–013.

U.S. EPA. (1986d) Addendum to the health assessment document for tetrachloroethylene (perchloroethylene). Updated carcinogenicity assessment for tetrachloroethylene (perchloroethylene, PERC, PCE). Review Draft. Office of Health and Environmental Assessment, Washington, DC. EPA–600/8–82/005FA.

U.S. EPA. (1986e) Analysis for polychlorinated dibenzeo-p-dioxins (PCDD) and dibenzofurans (PCDF) in human adipose tissue: method evaluation study. Office of Toxic Substances, Washington, DC. EPA–560/5–86–020.

U.S. EPA. (1987a). The total exposure assessment methodology (TEAM) study. Volume I: Summary and analysis. Office of Acid Deposition, Environmental Monitoring and Quality Assurance, Washington, DC. EPA–600/6–87/002a.

U.S. EPA. (1987b) Data quality objectives for remedial response activities. Example scenario: RI/FS activities at a site with contaminated soils and ground water. Office

of Emergency and Remedial Response and Office of Waste Programs Enforcement, Washington, DC. EPA/540/G-87/004.

U.S. EPA. (1987c) Selection criteria for mathematical models used in exposure assessments: surface water models. Office of Health and Environmental Assessment, Washington, DC. EPA/600/8-87/042.

U.S. EPA. (1987d) Pesticide assessment guidelines for applicator exposure monitoring-subdivision U. Exposure Assessment Branch, Hazard Evaluation Division, Office of Pesticide Programs, Washington, DC. EPA/540/9-87-127.

U.S. EPA. (1987e) Addendum to the health assessment document for trichloroethylene: updated carcinogenicity assessment for trichoroethylene. Office of Health and Environmental Assessment, Washington, DC. EPA/600/8-82/006FA.

U.S. EPA. (1988a) Total human exposure and indoor air quality: An automated bibliography (BLIS) with summary abstracts. Office of Acid Deposition, Monitoring, and Quality Assurance, Washington, DC. EPA/600/9-88-001.

U.S. EPA. (1988b) Laboratory data validation functional guidelines for evaluating organic analyses. Prepared for the Hazardous Site Evaluation Division, U.S. Environmental Protection Agency, Washington, DC. Prepared by the USEPA Data Review Work Group, February 1, 1988.

U.S. EPA. (1988c) Laboratory data validation functional guidelines for evaluating inorganic analyses. Prepared for the Hazardous Site Evaluation Division, U.S. Environmental Protection Agency, Washington, DC. Prepared by the USEPA Data Reivew Work Group, July 1, 1988.

U.S. EPA. (1988d) Selection criteria for mathematical models used in exposure assessments: Ground water models. Office of Health and Environmental Assessment, Washington, DC. EPA/600/8-88/075F.

U.S. Government Accounting Office. (1986). The nation's water: key unasnswered questions about the quality of rivers and streams. Washington, DC. GA01 PEMD-86-6.

U.S. Office of Management and Budget. (1988) 5 CFR Part 1320. Controlling paperwork burdens on the public: Regulatory changes reflecting amendments to the paperwork reduction act. Final rule. **Federal Register** 53:16617-16632.

Von Holstein, C.A.S.; Matheson, J.E. (1979) A manual for encoding probability distributions. SRI International, Menlo Park, CA.

Wallsten, T.S.; Budescu, D.V. (1983) Encoding subjective probabilities: a psychometric review. Manage. Sci. 29:151-173.

[FR Doc. 88-27687 Filed 12-1-88; 8:45 am]

BILLING CODE 6560-50-M